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(54) Title: CATALYST SYSTEM COMPRISING TRANSITION METAL AND IMIDAZOLINE-2-YLIDENE OR IMIDAZOLINE-2-YLIDENE AND ITS USE IN COUPLING REACTIONS

(57) Abstract: This invention provides a process for conducting reactions to form carbon-to-carbon or carbon-to-nitrogen bonds. The processes of the present invention make use of N-heterocyclic carbenes as ancillary ligands in various types of couplings of aryl halides and/or aryl pseudohalides. A Suzuki coupling, for example, can be carried out by mixing, in a liquid medium, at least one strong base; at least one aryl halide or aryl pseudohalide in which all substituents are other than boronic acid groups, wherein the aryl halide has, directly bonded to the aromatic ring(s), at least one halogen atom selected from the group consisting of a chlorine atom, a bromine atom, and an iodine atom; at least one arylboronic acid in which all substituents are other than chlorine atoms, bromine atoms, iodine atoms, or pseudohalide groups; at least one metal compound comprising at least one metal atom selected from nickel, palladium, and platinum, wherein the formal oxidation state of the metal is zero or two; and at least one N-heterocyclic carbene. One preferred type of N-heterocyclic carbene is an imidazoline-2-ylidene of the formula (I) wherein R<sup>1</sup> and R<sup>2</sup> are each, independently, alkyl or aryl groups having at least 3 carbon atoms, R<sup>3</sup> and R<sup>4</sup> are each, independently, a hydrogen atom, a halogen atom, or a hydrocarbyl group.

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**CATALYST SYSTEM COMPRISING TRANSITION METAL  
AND IMIDAZOLINE-2-YLIDENE OR IMIDAZOLIDINE-2-YLIDENE  
AND ITS USE IN COUPLING REACTIONS**

**TECHNICAL FIELD**

This invention relates to reactions involving carbon-to-carbon or carbon-to-nitrogen bond formation, which can be used for chemical synthesis in the polymer and the fine chemical industry.

**BACKGROUND**

The palladium catalyzed coupling reaction of aryl bromides, aryl iodides, and aryl pseudohalides (*e.g.*, triflates) is a general method employed for the formation of C-C and C-N bonds. Prior art methods generally cannot employ aryl chlorides as feedstock for these chemical transformations, and require the use of more expensive aryl bromides and aryl iodides. The use of aryl chlorides as chemical feedstock in coupling chemistry has proven difficult but would economically benefit a number of industrial processes. The few prior art methods that can employ aryl chlorides use expensive, air-sensitive phosphine ligands. See in this connection Old et al., *J. Am. Chem. Soc.*, 1998, **120**, 9722-9723, and Littke and Fu, *Angew. Chem. Int. Ed. Engl.*, 1998, **37**, 3387-3388, which describe phosphine-modified, palladium-mediated Suzuki coupling reactions which employ aryl chlorides as substrates. The use of a bulky phosphine (*e.g.*, tri(*tert*-butyl)phosphine) or phosphine-containing moiety (*e.g.*, di(cyclohexyl)phosphino) in ancillary ligation was shown to be fundamental in triggering the observed catalytic behavior. In addition, these phosphine ligands are often difficult to remove from the process product.

Nucleophilic N-heterocyclic carbenes, the imidazoline-2-ylidenes (sometimes commonly called imidazol-2-ylidenes) or so-called "phosphine mimics", have attracted considerable attention as possible alternatives for the widely used phosphine ligands in homogeneous catalysis. A primary advantage of these ligands is that an excess of the ligand is not required. It appears that these ligands do not dissociate from the metal center, thus preventing aggregation of the catalyst to yield the bulk metal. Further, these imidazoline-2-ylidene carbenes also appear to be more thermally stable than phosphines.

In fact, Herrmann et al., in *J. Organometallic Chem.*, 1998, **557**, 93-96, have reported Suzuki coupling activity using carbene ancillary ligands with aryl bromides and an activated

aryl chloride as substrates. While these carbene ligands are thermally stable, the reported reaction times were long, and the yield from the aryl chloride was relatively low.

### THE INVENTION

This invention provides new and highly advantageous catalyst compositions and processes for carrying out reactions to form C-C and C-N bonds. Thus, in one embodiment this invention provides a process which comprises mixing, in a liquid medium,

- i) at least one strong base;
- ii) at least one aryl halide or aryl pseudohalide, wherein the aryl halide has, directly bonded to the aromatic ring(s), at least one halogen atom selected from the group consisting of a chlorine atom, a bromine atom, and an iodine atom;
- iii) at least one transmetalating agent;
- iv) at least one metal compound comprising at least one metal atom selected from nickel, palladium, and platinum, wherein the formal oxidation state of the metal is zero or two; and
- v) at least one N-heterocyclic carbene.

The transmetalating agent is selected from the group consisting of at least one arylboronic acid in which all substituents are other than chlorine atoms, bromine atoms, iodine atoms, or pseudohalide groups; at least one primary amine and/or at least one secondary amine; at least one Grignard reagent; at least one organotin compound wherein the tin atom is quaternary, wherein one group bound to the tin atom is unsaturated at the alpha or beta position, and wherein each of the remaining groups bound to the tin atom is a saturated group; and at least one silane wherein the silicon atom is quaternary, wherein one group bound to the silicon atom is unsaturated at the alpha or beta position, and wherein each of the remaining groups bound to the silicon atom is a saturated hydrocarbyl or a saturated hydrocarbyloxy group; all with the proviso that (A) if the transmetalating agent is the arylboronic acid, all substituents of the aryl halide or aryl pseudohalide are other than boronic acid groups, (B) if the transmetalating agent is the primary and/or secondary amine, all substituents of the aryl halide or aryl pseudohalide are other than amino groups, (C) if the transmetalating agent is at least one Grignard reagent, the process is carried out in the absence of water and the strong base is optional, (D) if the transmetalating agent is the organotin compound, all substituents of the

aryl halide or aryl pseudohalide are other than stannyl groups, and (E) if the transmetalating agent is the silane, all substituents of the aryl halide or aryl pseudohalide are other than silyl groups. The carbene is selected from the group consisting of an imidazoline-2-ylidene wherein the 1 and 3 positions are each, independently, substituted by a secondary or tertiary group which has at least three atoms, or a protonated salt thereof; an imidazolidine-2-ylidene wherein the 1 and 3 positions are each, independently, substituted by a secondary or tertiary group which has at least three atoms, or a protonated salt thereof; a bis(imidazoline-2-ylidene) wherein a bridging moiety is bound to one nitrogen atom of each ring, and wherein the remaining two nitrogen atoms are each, independently, substituted by a secondary or tertiary group which has at least three atoms, or a protonated salt thereof; and a bis(imidazolidine-2-ylidene) wherein a bridging moiety is bound to one nitrogen atom of each ring, and wherein the remaining two nitrogen atoms are each, independently, substituted by a secondary or tertiary group which has at least three atoms, or a protonated salt thereof; and mixtures of two or more of the foregoing.

In one aspect, this invention provides a process for conducting Suzuki coupling reactions, wherein the transmetalating agent is at least one arylboronic acid in which all substituents are other than chlorine atoms, bromine atoms, iodine atoms, or pseudohalide groups. The catalyst system used in this embodiment of the invention exhibits the fastest reaction rate for Suzuki coupling observed to date, 3 times faster than the best reported rate for a phosphine-based catalyst system. The catalyst system of this embodiment also permits the use of aryl chlorides as substrates in Suzuki coupling reactions while eliminating the need for phosphine ligands. Furthermore, both electron-donating and electron-withdrawing substituents on the aryl halide or pseudohalide, the arylboronic acid, or both, in the Suzuki coupling reaction are well tolerated by the catalyst system, and provide the corresponding Suzuki coupling products in excellent yields.

In another aspect, this invention provides a process for conducting amination reactions, wherein the transmetalating agent is at least one primary amine and/or at least one secondary amine. This process uses a catalyst system comprising nickel, palladium, or platinum and imidazoline-2-ylidene or imidazolidine-2-ylidene, and permits the use of aryl chlorides as substrates in amination reactions while eliminating the need for phosphine ligands. Furthermore, both electron-donating and electron-withdrawing substituents on the



aryl halide or pseudohalide, the amine, or both, in the amination reaction are tolerated by the catalyst system used in the present invention, and provide the corresponding amination products in good yields.

In yet another aspect, this invention provides a process for conducting Kumada coupling reactions, wherein the transmetalating agent is at least one Grignard reagent. The catalyst system used in this embodiment of the invention permits the use of aryl chlorides as substrates in Kumada coupling reactions while eliminating the need for phosphine ligands. Furthermore, both electron-donating and electron-withdrawing substituents on the aryl halide or pseudohalide, the Grignard reagent, or both, in the Kumada coupling reaction are tolerated by the catalyst system used in the present invention, and provide the corresponding Kumada coupling products in excellent yields. Homocoupling of aryl pseudohalides is also feasible using the processes of this invention.

Still another aspect of this invention provides a process for conducting Stille coupling reactions, wherein the transmetalating agent is at least one organotin compound wherein the tin atom is quaternary, wherein one group bound to the tin atom is unsaturated at the alpha or beta position, and wherein each of the remaining groups bound to the tin atom is a saturated group. This embodiment of the present invention permits the use of aryl chlorides as substrates in Stille coupling reactions while eliminating the need for phosphine ligands. Furthermore, both electron-donating and electron-withdrawing substituents on the aryl halide or pseudohalide, the organotin compound, or both, in the Stille coupling reaction are tolerated by the catalyst system used in the present invention, and provide the corresponding Stille coupling products in good yields.

In another aspect, this invention provides provides a process for conducting coupling reactions of aryl halides using unsaturated silanes as the transmetalating agent. The catalyst system of this embodiment permits the use of aryl chlorides as substrates in these coupling reactions while eliminating the need for phosphine ligands. Furthermore, both electron-donating and electron-withdrawing substituents on the aryl halide or pseudohalide, the silane, or both, in the coupling reaction are well tolerated by the catalyst system of the present invention, and provide the corresponding heterocoupled products in excellent yields.

This invention also provides a catalyst system useful in all of the coupling reactions noted in this description. A feature of this aspect of the invention is the use of an

imidazoline-2-ylidene, an imidazolidine-2-ylidene, a bis(imidazoline-2-ylidene), and/or a bis(imidazolidine-2-ylidene) as part of the catalyst system. These N-heterocyclic carbenes and their corresponding salts are inexpensive and readily synthesized.

Thus, another embodiment of this invention is a composition which comprises at least one metal compound comprising at least one transition metal atom and at least one N-heterocyclic carbene or protonated salt of an N-heterocyclic carbene. The N-heterocyclic carbene is selected from the group consisting of i) an imidazoline-2-ylidene wherein the 1 and 3 positions are each, independently, substituted by an aromatic group in which each ortho position is, independently, substituted by a secondary or tertiary group which has at least three atoms, or a protonated salt of such an imidazoline-2-ylidene; ii) an imidazolidine-2-ylidene wherein the 1 and 3 positions are each, independently, substituted by an aromatic group in which each ortho position is, independently, substituted by a secondary or tertiary group having at least three atoms, or a protonated salt of such an imidazolidine-2-ylidene; iii) a bis(imidazoline-2-ylidene) wherein a bridging moiety is bound to one nitrogen atom of each ring, wherein the bridge formed by the bridging moiety has at least five atoms, and wherein the remaining two nitrogen atoms are each, independently, substituted by a secondary or tertiary group which has at least three atoms, or a protonated salt of such a bis(imidazoline-2-ylidene); iv) a bis(imidazolidine-2-ylidene) wherein a bridging moiety is bound to one nitrogen atom of each ring, wherein the bridge formed by the bridging moiety has at least five atoms, and wherein the remaining two nitrogen atoms are each, independently, substituted by a secondary or tertiary group which has at least three atoms, or a protonated salt of such a bis(imidazolidine-2-ylidene); and mixtures of two or more of the foregoing.

Another embodiment of this invention is a novel and highly efficacious group of N-heterocyclic carbenes which have the property or characteristic of greatly enhancing the effectiveness of the foregoing catalyst systems. The N-heterocyclic carbene is selected from the group consisting of i) an imidazoline-2-ylidene wherein the 1 and 3 positions are each, independently, substituted by an aromatic group in which each ortho position is, independently, substituted by a secondary or tertiary group which has at least three atoms, or a protonated salt of such an imidazoline-2-ylidene; ii) an imidazolidine-2-ylidene wherein the 1 and 3 positions are each, independently, substituted by an aromatic group in which each

ortho position is, independently, substituted by a secondary or tertiary group having at least three atoms, or a protonated salt of such an imidazolidine-2-ylidene; iii) a bis(imidazoline-2-ylidene) wherein a bridging moiety is bound to one nitrogen atom of each ring, wherein the bridge formed by the bridging moiety has at least five atoms, and wherein the remaining two nitrogen atoms are each, independently, substituted by a secondary or tertiary group which has at least three atoms, or a protonated salt of such a bis(imidazoline-2-ylidene); iv) a bis(imidazolidine-2-ylidene) wherein a bridging moiety is bound to one nitrogen atom of each ring, wherein the bridge formed by the bridging moiety has at least five atoms, and wherein the remaining two nitrogen atoms are each, independently, substituted by a secondary or tertiary group which has at least three atoms, or a protonated salt of such a bis(imidazolidine-2-ylidene); and mixtures of two or more of the foregoing.

Significantly better yields are obtained, often in shorter reaction times, with catalyst systems comprising the N-heterocyclic carbenes of this invention than with catalyst systems which utilize N-heterocyclic carbenes that do not have such features.

Further embodiments and features of this invention will be apparent from the ensuing description and appended claims. For ease of reference only, the following details of various aspects of this invention will be set forth under subheadings immediately following which will be, respectively, the details pertinent to the embodiment identified by the subheading. The subheadings themselves are intended to aid the reader, but shall not be construed as otherwise limiting the present invention.

#### Arylboronic Acid as Transmetalating Agent

The liquid medium for the processes of this embodiment of the invention can include any of a wide range of solvents, and mixtures of solvents are also usable. The exclusion of water is not necessary, but is preferred. Types of solvents that can be used include hydrocarbons, ethers, amides, ketones, and alcohols. Polar solvents are preferred; ethers are a more preferred solvent type. Ethers that may be used include, for example, diethyl ether, di-*n*-propyl ether, diisopropyl ether, *tert*-butyl ethyl ether, diheptyl ether, 1,3-dioxolane, 1,4-dioxane, tetrahydrofuran, methyltetrahydrofuran, glyme (the dimethyl ether of ethylene glycol), diglyme (the dimethyl ether of diethylene glycol), and the like. Cyclic ethers and

polyethers are preferred; a highly preferred ether is 1,4-dioxane.

A large variety of strong bases are suitable for use in the processes of this embodiment of the invention. Generally, these are inorganic bases. Alkali metal salts are a preferred group of inorganic bases. Examples of suitable alkali metal salts include, but are not limited to, sodium acetate, sodium bicarbonate, sodium *tert*-butoxide, sodium oxide, sodium tetrafluoroborate, potassium acetate, potassium carbonate, potassium *tert*-butoxide, potassium nitrite, potassium phosphate, potassium sulfite, potassium hexafluorophosphate, cesium acetate, cesium bicarbonate, cesium carbonate, cesium fluoride, cesium nitrate, and cesium sulfate. Alkali metal salts of carboxylic acid anions (*e.g.*, acetate, trifluoroacetate, citrate, formate, oxalate, propionate, tartrate, *etc.*) are also suitable for use as the inorganic base in this invention. More preferred are salts of potassium and cesium; most preferred are cesium salts. The most highly preferred inorganic base is cesium carbonate. Choice(s) of inorganic base will vary with the particular system of aryl halide or pseudohalide and arylboronic acid involved. Amine bases are generally not preferred because, to date, they appear to poison the catalyst system of the invention.

Directly bonded to the aromatic ring(s) of the aryl halide or pseudohalide (*i.e.*, aryl halide or aryl pseudohalide) is at least one halogen atom selected from a chlorine atom, a bromine atom, and an iodine atom, or at least one pseudohalide group. The term "pseudohalide group" includes such groups as *p*-toluenesulfonate (tosylate), and trifluoromethanesulfonate (triflate). The aryl halide or pseudohalide can have two or more such halogen atoms with an atomic number greater than nine and/or pseudohalide groups, including combinations of halogen atoms and pseudohalide groups. However, when two or more such groups are present, the halogen atoms with an atomic number greater than nine and/or pseudohalide groups should all be different from each other. For example, when two such substituents are present, they may be a chlorine atom and a bromine atom, or an iodine atom and a tosylate group, or *etc.* It is preferred that there is only one chlorine atom, bromine atom, iodine atom, or pseudohalide group directly bound to the aryl ring of the aryl halide or pseudohalide. Aryl chlorides are more preferred as the aryl halide reactants. To prevent self-reaction, it is preferred that boronic acid groups are not present on the aryl halide or pseudohalide.

The aryl moiety for the aryl halide or pseudohalide can be homocyclic or heterocyclic.

Examples of suitable homocyclic aryl moieties include, but are not limited to, benzene, naphthalene, anthracene, phenanthrene, pyrene, biphenyl, acenaphthalene, fluorene, and indene. Heterocyclic aryl moieties that can be used include, for example, furan, thiophene, oxathiolane, thianthrene, isobenzofuran, phenoxathiin, and the like. Nitrogen-containing heterocycles, such as pyridine, indole, and isoxazole may have an effect on the catalyst system similar to that of amine bases, as described above, and thus are not preferred. Benzene is a preferred aryl moiety for the aryl halide or pseudohalide.

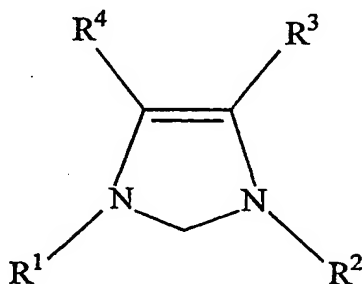
For the aryl halide or pseudohalide, substituents other than a chlorine atom, a bromine atom, an iodine atom, and/or a pseudohalide group that may be present on the aromatic ring(s) include, but are not limited to, hydrogen atoms, fluorine atoms, nitro groups, hydrocarbyl groups, alkoxy groups, perfluorohydrocarbyl groups, silyl groups, ether groups, ketone groups, and ester groups. When hydrocarbyl groups are present, they are preferably C<sub>1</sub> to C<sub>18</sub> alkyl groups or C<sub>6</sub> to C<sub>20</sub> aryl or aralkyl groups. Examples of suitable hydrocarbyl groups are methyl, ethyl, isopropyl, *tert*-butyl, cyclopentyl, methylcyclohexyl, decyl, phenyl, tolyl, xylyl, benzyl, naphthyl, and tetrahydronaphthyl. Alkoxy group substituents preferably have C<sub>1</sub> to C<sub>6</sub> alkyl moieties. Some examples of alkoxy groups are methoxy, ethoxy, isopropoxy, methylcyclopentoxy, and cyclohexoxy. Perfluorohydrocarbyl groups include alkyl and aryl perfluorocarbons; suitable perfluorohydrocarbyl groups are, for example, trifluoromethyl, pentafluoroethyl, pentafluorophenyl, and heptafluoronaphthyl. Substituent silyl groups preferably have C<sub>1</sub> to C<sub>18</sub> alkyl groups or C<sub>6</sub> to C<sub>20</sub> aryl or aralkyl groups, and examples include trimethylsilyl, triisopropylsilyl, *tert*-butyl(dimethyl)silyl, tridecylsilyl, and triphenylsilyl. The substituents preferred for the aryl halide or pseudohalide will depend on the product that is desired.

It is preferred that the arylboronic acid contains only one boronic acid group directly bonded to the aromatic ring(s), which may prevent mixtures of products from forming. It is recognized that more than one boronic acid group may be present when a mixture of products is desired. To prevent self-reaction, it is also preferred that chlorine atoms, bromine atoms, iodine atoms, and/or pseudohalide groups are not present on the aromatic ring(s) of the arylboronic acid. In other words, the arylboronic acid is preferably devoid of halogen atoms with an atomic number greater than nine, and is also preferably devoid of pseudohalide groups. However, one or more fluorine atoms can be present on the aromatic ring(s).

The aryl moiety of the arylboronic acid can be homocyclic or heterocyclic, as described for the aryl halide or pseudohalide. For the arylboronic acid, the preferred aryl moieties are benzene and naphthalene. Substituents on the aryl ring, again as described for the aryl halide or pseudohalide, can be hydrogen atoms, fluorine atoms, nitro groups, hydrocarbyl groups, alkoxy groups, perfluorohydrocarbyl groups, silyl groups, ether groups, ketone groups, and ester groups. Preferred substituents for the arylboronic acid depend on the desired product.

The metal compound comprises at least one metal atom selected from nickel, palladium, and platinum having a formal oxidation state of zero or two, and is sometimes referred to hereinafter as the metal compound. Inorganic salts of nickel, palladium, or platinum that can be used include the bromides, chlorides, fluorides, iodides, cyanides, nitrates, sulfides, sulfites, and sulfates. Organic nickel, palladium, or platinum compounds that may be used include complexes and salts such as the carboxylates, *e.g.*, the acetates or propionates, *etc.* Suitable nickel compounds include bis(1,5-cyclooctadiene)nickel, nickel acetate, nickel oxalate, nickel phosphate, nickel stearate, nickel acetylacetonate, nickel tetrafluoroborate, nickel thiocyanate, nickel carbonate, and nickel sulfamate. Examples of palladium compounds include  $\text{Pd}(\text{OAc})_2$ , palladium(II) chloride,  $\text{Pd}(\text{CH}_3\text{CN})_4(\text{BF}_4)_2$ , tris(dibenzylideneacetone)dipalladium(0) [which is also referred to herein as dipalladium tris(dibenzylideneacetone)], and palladium trifluoroacetate. Platinum compounds that can be used include platinum acetylacetonate and platinum chloride. Nickel and palladium compounds are preferred; more preferred are compounds of palladium. Palladium compounds such as palladium acetate and tris(dibenzylideneacetone)dipalladium(0) are most preferred.

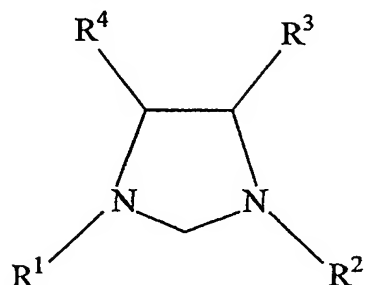
Preferred types of N-heterocyclic carbenes are imidazoline-2-ylidenes of the formula



or protonated salts thereof, wherein R<sup>1</sup> and R<sup>2</sup> are each, independently, alkyl or aryl groups

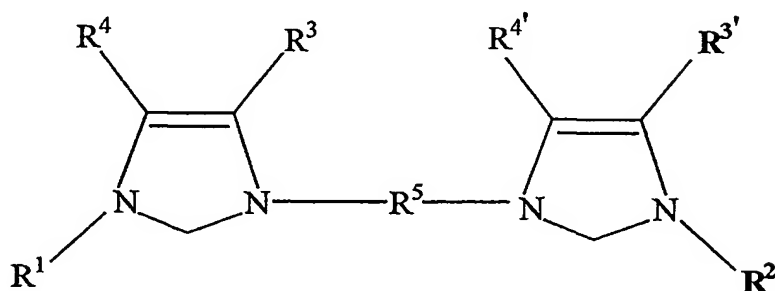
having at least 3 carbon atoms,  $R^3$  and  $R^4$  are each, independently, a hydrogen atom, a halogen atom, or a hydrocarbyl group;

imidazolidine-2-ylidenes of the formula

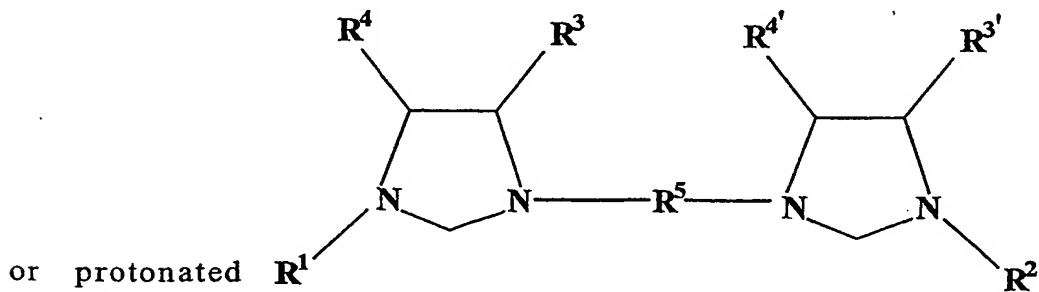


or protonated salts thereof, wherein  $R^1$ ,  $R^2$ ,  $R^3$ , and  $R^4$  are as defined for the imidazoline-2-ylidenes;

bis(imidazoline-2-ylidene)s of the formula



or protonated salts thereof, wherein  $R^1$ ,  $R^2$ ,  $R^3$ , and  $R^4$  are as defined for the imidazoline-2-ylidenes, wherein  $R^{3'}$  and  $R^{4'}$  are as defined for  $R^3$  and  $R^4$  for the imidazoline-2-ylidenes, and wherein  $R^5$  is a bridging group that links the two imidazoline rings;  
bis(imidazolidine-2-ylidene)s of the formula



salts thereof, wherein  $R^1$ ,  $R^2$ ,  $R^3$ , and  $R^4$  are as defined for the imidazoline-2-ylidenes, wherein  $R^{3'}$  and  $R^{4'}$  are as defined for  $R^3$  and  $R^4$  for the imidazoline-2-ylidenes, and wherein  $R^5$  is a bridging group that links the two imidazolidine rings.

$R^1$  and  $R^2$  are preferably sterically bulky groups. Suitable groups include, but are not limited to, isopropyl, *sec*-butyl, *tert*-butyl, 2,2-dimethylpropyl (neopentyl), cyclohexyl, norbornyl, adamantyl, tolyl, 3,5-dimethylphenyl, 2,4,6-trimethylphenyl, 2,6-diisopropylphenyl, and triphenylmethyl. Preferred groups are *tert*-butyl, 2,4,6-trimethylphenyl, 2,6-diisopropylphenyl, and triphenylmethyl. Most preferred for both  $R^1$  and  $R^2$  are the 2,4,6-trimethylphenyl and 2,6-diisopropylphenyl groups.

Examples of suitable  $R^3$ ,  $R^4$ ,  $R^{3'}$ , and  $R^{4'}$  groups include chlorine atoms, bromine atoms, hydrogen atoms, hydrocarbyl groups, and the like. When hydrocarbyl groups are present, they are preferably  $C_1$  to  $C_{18}$  alkyl groups or  $C_6$  to  $C_{20}$  aryl or aralkyl groups. Examples of suitable hydrocarbyl groups are methyl, ethyl, isopropyl, *tert*-butyl, cyclopentyl, methylcyclohexyl, decyl, phenyl, tolyl, xylyl, benzyl, naphthyl, and tetrahydronaphthyl. Chlorine atoms and hydrogen atoms are preferred groups. Most preferred for all substituents  $R^3$ ,  $R^4$ ,  $R^{3'}$ , and  $R^{4'}$  are hydrogen atoms.

$R^5$  in both the formula for the bis(imidazoline-2-ylidene)s and the bis(imidazolidine-2-ylidene)s of this invention can be selected from a large variety of moieties, including alkylene groups, arylene groups, and silylene groups. Atoms that can form the bridge include, but are not limited to, carbon, nitrogen, oxygen, silicon, and sulfur. Examples of suitable bridging moieties include methylene ( $-\text{CH}_2-$ ), substituted methylene, ethylene ( $-\text{CH}_2\text{CH}_2-$ ), substituted ethylene, silylene ( $>\text{SiR}_2$ ), benzo ( $\text{C}_6\text{H}_4<$ ), substituted benzo, biphenylene, substituted biphenylene, binaphthylene, and substituted binaphthylene. Heterocyclic aromatic moieties such as, for example, pyridine, pyrimidine, pyrazine, pyridazine, furan, thiophene, oxathiolane, thianthrene, isobenzofuran, phenoxathiin, isothiazole, phenoxazine, and the like, can also form the bridge. Preferred  $R^5$  moieties include biphenylene, binaphthylene, and substituted benzo, with substituted benzo being more preferred. Highly preferred is benzo substituted with methyl groups. The bridge preferably has at least four atoms, and more preferably has from four to eight atoms. While better results have been observed with longer bridges, it is possible that judicious choices for  $R^1$ ,  $R^2$ ,  $R^3$ ,  $R^4$ ,  $R^{3'}$ , and  $R^{4'}$  may improve



results for short bridges.

Without being bound by theory, it appears from thermochemical studies that the electron-donating ability of many of the imidazoline-2-ylidene carbene ligands is better than that of tri(cyclohexyl)phosphine and the steric demand of these carbene ligands is greater than that of tri(cyclohexyl)phosphine. This suggests that the N-heterocyclic carbene should possess steric bulk sufficient to stabilize both the free carbene and to stabilize reaction intermediates. However, imidazoline-2-ylidene carbenes and imidazolidine-2-ylidene carbenes are considerably less stable to air and moisture than their corresponding protonated imidazolinium and imidazolidinium salts. Thus, a highly preferred embodiment of this invention involves generation of the imidazoline-2-ylidene *in situ* from the corresponding imidazolinium salt (similarly so for the imidazolidine-2-ylidene and the corresponding imidazolidinium salt); this removes the need to handle the N-heterocyclic carbene ligands in an inert atmosphere. Protonated salts of the imidazoline-2-ylidene carbenes and imidazolidine-2-ylidene carbenes are monoprotated, while the protonated salts of the bis(imidazoline-2-ylidene)s and the bis(imidazolidine-2-ylidene)s are diprotated. Suitable counterions for the protonated salts are virtually limitless, but halides are preferred counterions. The most preferred counterions are chloride and bromide. The imidazolinium salts are straightforward to synthesize and are air-stable. While the absence of oxygen is not necessary when using a protonated salt of an imidazoline-2-ylidene carbene or an imidazolidine-2-ylidene carbene, it is preferred. When using a neutral carbene, the absence of oxygen is necessary. In any instance where oxygen is excluded, the presence of an inert gas such as nitrogen, helium, or argon is preferred.

The aryl halide or pseudohalide and the arylboronic acid may be employed in an ideal molar ratio of about 1:1 when using an aryl halide or pseudohalide that has only one halogen atom (other than a fluorine atom) or pseudohalide group; or either reagent may be used in excess. It is preferred to use the arylboronic acid in an excess such that the molar ratio of aryl halide or pseudohalide to arylboronic acid is in the range of from about 1:1 to about 1:3 when using an aryl halide or pseudohalide that has only one halogen atom (other than a fluorine atom) or pseudohalide group. When the aryl halide or pseudohalide has more than one halogen atom (other than fluorine) and/or pseudohalide group, reactions may be carried out in sequence. An arylboronic acid will react first at the site of the more reactive substituent,

*e.g.*, at iodine before bromine. Reaction at only the site of the more reactive substituent(s) can be performed. In reactions carried out in sequence where the arylboronic acids are different, each should be added separately. It is preferred to allow one reaction to finish before the addition of the next arylboronic acid. When different arylboronic acids are used, it is preferred to use close to the ideal molar ratio of aryl halide or pseudohalide to arylboronic acid to minimize undesirable side products.

A suitable molar ratio of aryl halide or pseudohalide to strong base is in the range of from about 1:1 to about 1:5. A more preferred molar ratio of aryl halide or pseudohalide to strong base is in the range of from about 1:1 to about 1:3.

Normally, the molar ratio of metal atoms of the metal compound to aryl halide or pseudohalide molecules is in the range of from about 0.01:1 to about 0.05:1; a preferred molar ratio of metal atoms of metal compound to aryl halide or pseudohalide molecules is in the range of from about 0.02:1 to about 0.04:1. For the metal compound and the carbene ligands, the molar ratio of metal atoms of the metal compound to carbene molecules is in the range of from about 1:0.5 to about 1:5, and more preferably in the range of from about 1:1 to about 1:3.

The order of addition of the various components to a reaction vessel is not of particular importance. Premixing of the components of the catalyst system is not necessary; however, it is preferred that the catalyst system is premixed. To premix the components of the catalyst system, the metal compound, the N-heterocyclic carbene (salt or neutral compound), and the strong base are mixed together after being added in no particular order to a reaction vessel. The mixing time (activation period) for these components on the laboratory scale may be very short, *e.g.*, five minutes or less, but a preferred mixing time is in the range of from about fifteen minutes to about sixty minutes.

If a premixed catalyst system is used, the aryl halide or pseudohalide and the arylboronic acid may be added to the same reaction vessel, or the premixed catalyst system can be transferred to a different vessel in which the reaction is to take place. Use of the same vessel for premixing the catalyst system and conducting the reaction is preferred.

When the components of the catalyst system are not premixed, the strong base, aryl halide or pseudohalide, the arylboronic acid, the metal compound, the liquid medium, and the N-heterocyclic carbene (salt or neutral compound) are added in any order to the reaction

vessel.

Once all of the components are present in the same reaction vessel, the mixture may be heated, provided that the temperature does not exceed the thermal decomposition temperature of the catalyst system or the products of the reaction. Preferred temperatures are in the range of from about 20°C to about 150°C; more preferred temperatures are in the range of from about 20°C to about 110°C. When the aryl halide or pseudohalide is an aryl chloride, an aryl triflate, or an aryl tosylate, heat is usually necessary to drive the reaction. Preferred temperatures when the aryl halide or pseudohalide is an aryl chloride, an aryl triflate, or an aryl tosylate are in the range of from about 40°C to about 150°C. When the aryl halide or pseudohalide is an aryl bromide or an aryl iodide, the reaction(s) proceeds easily at room temperature, although heat may speed the reaction. For aryl bromides and aryl iodides, preferred temperatures are in the range of from about 20°C to about 70°C.

While not necessary when using protonated salts of N-heterocyclic carbenes, the absence of oxygen and water is preferred when conducting the processes of this invention. Conversely, the exclusion of oxygen and water is generally necessary when neutral carbenes are used. The presence of an inert gas such as argon or nitrogen is preferred when oxygen and/or water are excluded. The reaction mixture is normally agitated. A preferred contact time for the components of the reaction is in the range of from about one hour to about forty-eight hours. More preferably, the contact time is from about one hour to about twenty-four hours.

The following examples are presented for purposes of illustration, and are not intended to impose limitations on the scope of this embodiment of the invention.

## EXAMPLES 1-8

### GENERAL PROCEDURES

**Reagents.** All aryl chlorides (Aldrich Chemical Company), arylboronic acids (Aldrich), triethylamine (J.T. Baker Incorporated), Na<sub>2</sub>CO<sub>3</sub> (EM Science), K(CH<sub>3</sub>CO<sub>2</sub>) (EM Science), K<sub>2</sub>CO<sub>3</sub> (EM Science), CsF (Aldrich), Cs<sub>2</sub>CO<sub>3</sub> (Aldrich), and Pd<sub>2</sub>(dibenzylideneacetone)<sub>3</sub> were used as received. 1,4-Dioxane was distilled from Na/benzophenone ketyl. Flash chromatography was performed on silica gel 60 (230-400

mesh; Natland International Corporation).

1,3-bis(2,4,6-trimethylphenyl)imidazoline-2-ylidene and 1,3-Bis(2,4,6-trimethylphenyl)imidazolium chloride were prepared according to reported procedures in U.S. Patent No. 5,077,414, and/or Arduengo, A. J. III., Dias, H.V.R.; Harlow, R.L. and Kline, M. *J. Am. Chem. Soc.*, 1992, 114, 5530-5534.

**Analyses.** All reactions were monitored by thin layer chromatography (TLC).  $^1\text{H}$  and  $^{13}\text{C}$  nuclear magnetic resonance (NMR) spectra were recorded on a 300 MHz NMR spectrometer (Varian, Incorporated) or 400 MHz NMR spectrometer (Varian) at ambient temperature in  $\text{CDCl}_3$  (Cambridge Isotope Laboratories, Incorporated). All of the products, which are known compounds, had  $^1\text{H}$  NMR spectra identical with literature data.

**Conditions.** All reactions were carried out under an atmosphere of argon in oven-dried glassware with magnetic stirring, unless otherwise indicated.

### EXAMPLE 1

For each run, a Schlenk tube was charged with  $\text{Pd}_2(\text{dibenzylideneacetone})_3$  (14 mg, 0.015 mmol), 1,3-bis(2,4,6-trimethylphenyl)imidazolium chloride (10 mg, 0.03 mmol), base (2.00 equivalents), and a magnetic stirring bar. After a 30 minute catalyst activation period, 1,4-dioxane (3 mL), 4-chlorotoluene (1.0 mmol), and phenylboronic acid (1.5 mmol) were added in turn to the Schlenk tube. The Schlenk tube was placed in a  $80^\circ\text{C}$  oil bath and the mixture was stirred for a number of hours. The mixture was then allowed to cool to room temperature. The reaction mixture was purified either directly by flash chromatography, or filtered through a pad of Celite® (desiccant), concentrated, and then purified by flash chromatography.

The base used in each run is listed in Table 1. All of the yields reported in Table 1 are of the heterocoupling product, and are the average of two runs. Reaction times reported in Table 1 do not include the 30 minute catalyst activation period.

TABLE 1

Run	Base	Reaction time	Isolated yield
a	$\text{Et}_3\text{N}$	24 hr.	<5% <sup>a,b</sup>
b	$\text{Na}_2\text{CO}_3$	43 hr.	6% <sup>a</sup>
c	KOAc	43 hr.	42% <sup>a</sup>

d	K <sub>2</sub> CO <sub>3</sub>	24 hr.	53%
e	CsF	2 hr.	65%
f	Cs <sub>2</sub> CO <sub>3</sub>	1.5 hr.	96%

<sup>a</sup>4-Chlorotoluene was not completely consumed within the indicated reaction time (by TLC).

<sup>b</sup> Precipitation of Pd black was observed.

## EXAMPLE 2

Reagents, analyses, and procedures were as described in Example 1, except as follows. The base for all runs was Cs<sub>2</sub>CO<sub>3</sub> (652 mg, 2.00 mmol). Several different aryl chlorides (1.0 mmol each) and arylboronic acids (1.5 mmol each) were used. The mixture in the Schlenk tube was stirred for 1.5 hours in the oil bath. The aryl chlorides and arylboronic acids used in each run are listed in Table 2. All of the yields reported in Table 2 are of the heterocoupling product, and are the average of two runs.

TABLE 2

Run	Aryl chloride	Arylboronic acid	Isolated yield
a	4-Chlorotoluene	Phenylboronic acid	96%
b	4-Chlorotoluene	Phenylboronic acid	97% <sup>a</sup>
c	4-Chlorotoluene	4-Methoxyphenylboronic acid	99%
d	4-Chlorotoluene	2-Methoxyphenylboronic acid	88%
e	4-Chlorotoluene	3-Methoxyphenylboronic acid	91%
f	4-Chlorobenzene	4-Methoxyphenylboronic acid	99%
g	1,4-Dimethyl-2-chlorobenzene	Phenylboronic acid	89%
h	1-Methoxy-4-chlorobenzene	Phenylboronic acid	93%
i	Methyl-4-chlorobenzoate	Phenylboronic acid	99%

<sup>a</sup>6.0 mol % of 1,3-bis(2,4,6-trimethylphenyl)imidazolinium chloride was used.

## EXAMPLE 3

Reagents, analyses, and procedures were as described in Example 1, except as follows. The base (2.00 mmol) was either  $\text{Cs}_2\text{CO}_3$  or  $\text{K}_2\text{CO}_3$ ; the metal compound was either  $\text{Pd}(\text{CH}_3\text{CO}_2)_2$  (5.8mg, 0.025 mmol) or  $\text{Pd}_2(\text{dibenzylideneacetone})_3$  (18.8mg, 0.01 mmol); and the N-heterocyclic carbene was 1,3-bis(2,6-diisopropylphenyl)imidazolinium chloride (106 mg, 0.03 mmol). The aryl halide or pseudohalide in all runs was 4-methylphenyl *p*-toluenesulfonate (1.0 mmol). Several different arylboronic acids (1.5 mmol each) were used. The mixture in the Schlenk tube was stirred for 1.5 hours in the oil bath. The arylboronic acid, metal compound, and base used in each run are listed in Table 3. All of the yields reported in Table 3 are of the heterocoupling product, and are the average of two runs.

TABLE 3

Run	Base	Metal compound	Arylboronic acid	Isolated yield
a	$\text{Cs}_2\text{CO}_3$	$\text{Pd}(\text{CH}_3\text{CO}_2)_2$	Phenylboronic acid	94%
b	$\text{K}_2\text{CO}_3$	$\text{Pd}(\text{CH}_3\text{CO}_2)_2$	4-Methylphenylboronic acid	4.6%
c	$\text{Cs}_2\text{CO}_3$	$\text{Pd}_2(\text{dibenzylideneacetone})_3$	Phenylboronic acid	94%
d	$\text{K}_2\text{CO}_3$	$\text{Pd}_2(\text{dibenzylideneacetone})_3$	4-Methylphenylboronic acid	98%

## EXAMPLE 4

Reagents, analyses, and procedures were as described in Example 1, except as follows. The base (2.00 mmol) was either  $\text{Cs}_2\text{CO}_3$  or  $\text{K}_2\text{CO}_3$ ; the metal compound was either  $\text{Pd}(\text{CH}_3\text{CO}_2)_2$  (5.6mg, 0.025 mmol) or  $\text{Pd}_2(\text{dibenzylideneacetone})_3$  (18.8mg, 0.01 mmol); and the N-heterocyclic carbene was 1,3-bis(2,6-diisopropylphenyl)imidazolinium chloride (106 mg, 0.03 mmol). Several different aryl triflates (1.0 mmol each) and arylboronic acids (1.5 mmol each) were used. The mixture in the Schlenk tube was stirred for 1.5 hours in the oil bath. The aryl triflate, arylboronic acid, metal compound, and base used in each run are listed in Table 4. All of the yields reported in Table 4 are of the heterocoupling product, and are the average of two runs.

TABLE 4

Run	Base	Metal compound	Aryl Triflate	Arylboronic acid	Isolated yield
a	Cs <sub>2</sub> CO <sub>3</sub>	Pd(CH <sub>3</sub> CO <sub>2</sub> ) <sub>2</sub>	4-methoxyphenyl triflate	Phenylboronic acid	86%
b	K <sub>2</sub> CO <sub>3</sub>	Pd(CH <sub>3</sub> CO <sub>2</sub> ) <sub>2</sub>	4-methoxyphenyl triflate	4-Methylphenylboronic acid	75%
c	Cs <sub>2</sub> CO <sub>3</sub>	Pd(CH <sub>3</sub> CO <sub>2</sub> ) <sub>2</sub>	4-methoxyphenyl triflate	4-Methoxyphenylboronic acid	81%
d	K <sub>2</sub> CO <sub>3</sub>	Pd(CH <sub>3</sub> CO <sub>2</sub> ) <sub>2</sub>	Phenyl triflate	Phenylboronic acid	52%
e	K <sub>2</sub> CO <sub>3</sub>	Pd(CH <sub>3</sub> CO <sub>2</sub> ) <sub>2</sub>	Phenyl triflate	4-Methylphenylboronic acid	99+%
f	Cs <sub>2</sub> CO <sub>3</sub>	Pd(CH <sub>3</sub> CO <sub>2</sub> ) <sub>2</sub>	Phenyl triflate	4-Methoxyphenylboronic acid	85%
g	Cs <sub>2</sub> CO <sub>3</sub>	Pd(CH <sub>3</sub> CO <sub>2</sub> ) <sub>2</sub>	4-CH <sub>3</sub> CO <sub>2</sub> -phenyl triflate	Phenylboronic acid	76%
h	K <sub>2</sub> CO <sub>3</sub>	Pd(CH <sub>3</sub> CO <sub>2</sub> ) <sub>2</sub>	4-CH <sub>3</sub> CO <sub>2</sub> -phenyl triflate	4-Methylphenylboronic acid	93%
i	Cs <sub>2</sub> CO <sub>3</sub>	Pd(CH <sub>3</sub> CO <sub>2</sub> ) <sub>2</sub>	4-CH <sub>3</sub> CO <sub>2</sub> -phenyl triflate	4-Methoxyphenylboronic acid	77%
j	Cs <sub>2</sub> CO <sub>3</sub>	Pd <sub>2</sub> (dibenzylideneacetone) <sub>3</sub>	4-methoxyphenyl triflate	Phenylboronic acid	97%
k	Cs <sub>2</sub> CO <sub>3</sub>	Pd <sub>2</sub> (dibenzylideneacetone) <sub>3</sub>	4-methoxyphenyl triflate	4-Methylphenylboronic acid	98%
l	K <sub>2</sub> CO <sub>3</sub>	Pd <sub>2</sub> (dibenzylideneacetone) <sub>3</sub>	Phenyl triflate	Phenylboronic acid	98%
m	Cs <sub>2</sub> CO <sub>3</sub>	Pd <sub>2</sub> (dibenzylideneacetone) <sub>3</sub>	Phenyl triflate	4-Methylphenylboronic acid	99%
n	K <sub>2</sub> CO <sub>3</sub>	Pd <sub>2</sub> (dibenzylideneacetone) <sub>3</sub>	4-CH <sub>3</sub> CO <sub>2</sub> -phenyl triflate	Phenylboronic acid	55%
o	Cs <sub>2</sub> CO <sub>3</sub>	Pd <sub>2</sub> (dibenzylideneacetone) <sub>3</sub>	4-CH <sub>3</sub> CO <sub>2</sub> -phenyl triflate	4-Methylphenylboronic acid	97%

## EXAMPLE 5

Reagents, analyses, and procedures were as described in Example 1, except as follows. The base was Cs<sub>2</sub>CO<sub>3</sub> (652 mg, 2.00 mmol); the metal compound was bis(1,5-cyclooctadiene)nickel (8.3mg, 0.03 mmol, or 16.7mg, 0.06 mmol); and the N-heterocyclic carbene was 1,3-bis(2,6-diisopropylphenyl)imidazolinium chloride (106 mg, 0.03 mmol). Several different aryl chlorides (1.0 mmol each) and aryl triflates (1.0 mmol each) were used. The arylboronic acid for all runs was phenylboronic acid (1.5 mmol). The mixture in the Schlenk tube was stirred for 48 hours in the oil bath. The aryl chloride or aryl triflate and the amount of bis(1,5-cyclooctadiene)nickel used in each run are listed in Table 5. All of the yields reported in Table 5 are of the heterocoupling product, and are the average of two runs.

TABLE 5

Run	Amount of bis(1,5-cyclooctadiene)nickel	Aryl chloride or aryl triflate	Isolated yield
a	0.03 mmol	4-Chlorotoluene	10%
b	0.03 mmol	1-Methoxy-4-chlorobenzene	5%

c	0.03 mmol	Methyl-4-chlorobenzoate	10%
d	0.06 mmol	4-Chlorotoluene	8%
e	0.06 mmol	Methyl-4-chlorobenzoate	48%
f	0.06 mmol	4-methylphenyl triflate	NR% <sup>a</sup>
g	0.06 mmol	4-methylphenyl triflate	<5%
h	0.06 mmol	4-methoxyphenyl triflate	12%
i	0.06 mmol	4-CH <sub>3</sub> CO <sub>2</sub> -phenyl triflate	5%

<sup>a</sup>NR = no reaction; no carbene was used in this run.

### EXAMPLE 6

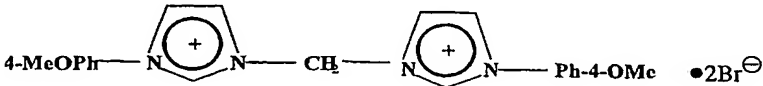
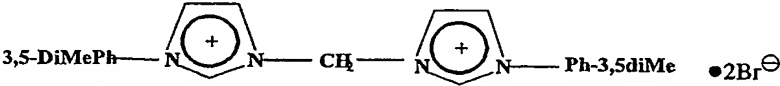
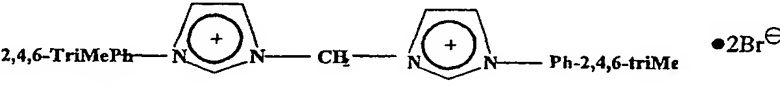
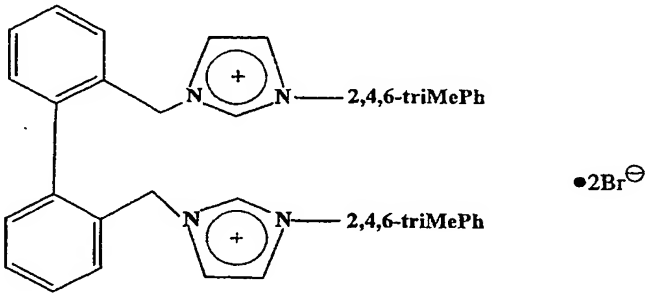
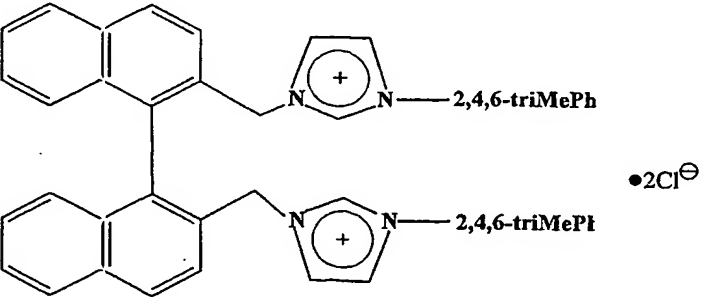
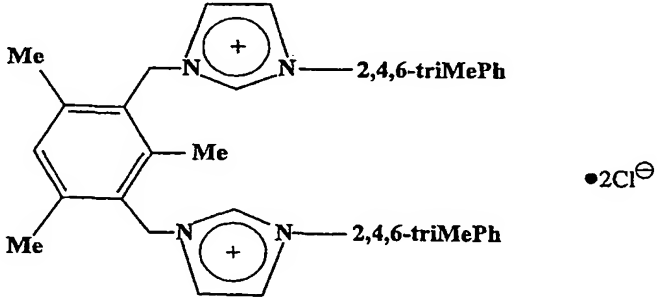
Six bis(imidazolinium) salts (see Table 6) were prepared by heating the dibromide or dichloride of the molecule intended to be the bridging moiety with two equivalents of an 1-aryl-imidazol in xylene. As an example, a mixture of dibromomethane (1.0 mmol) and N-(3,5-dimethylphenyl)imidazoline (2.0 mmol) was heated in xylene (5 mL) at 140 °C for 2 days. This afforded the salt shown in Run B of Table 6 in 70% yield. Alternatively, a mixture of 1,3-di( $\alpha$ -chloromethyl)-2,4,6-trimethylbenzene (1.0 mmol) and N-(2,4,6-trimethylphenyl)imidazoline (2.0 mmol) was heated in xylene (5 mL) at 120 °C for 48 hours and furnished the salt shown in Run F of Table 6 in 85% yield.

### EXAMPLE 7

The procedure used in all runs of this example are as follows: A Schlenk tube was charged with Pd(CH<sub>3</sub>CO<sub>2</sub>)<sub>2</sub> (5.6 mg, 0.025 mmol), one of the carbenes prepared in Example 6 (0.025 mmol), Cs<sub>2</sub>CO<sub>3</sub> (2.00 equivalents), and a magnetic stirring bar. After a 30 minute catalyst activation period, 1,4-dioxane (3 mL), 4-chlorotoluene (1.0 mmol), and phenylboronic acid (1.5 mmol) were added in turn to the Schlenk tube. The Schlenk tube was placed in a 80 °C oil bath and stirred for a number of hours. The mixture was then allowed to cool to room temperature. The bis(imidazoline-2-ylidene) used in each run are listed in Table 6. All of the yields reported in Table 6 are of the heterocoupling product, and are the average of two runs.



TABLE 6

Run	Bis(imidazolium) salt	Reaction time	Isolated yield
A		24 hr.	trace <sup>a</sup>
B		24 hr.	< 5% <sup>a</sup>
C		6 hr.	32% <sup>a</sup>
D		4 hr.	65% <sup>a</sup>
E		4 hr.	87%
F		1.5 hr.	99%

<sup>a</sup>4-Chlorotoluene was not completely consumed and precipitation of Pd black was observed.

## EXAMPLE 8

The procedure used in all runs of this Example was as follows: A Schlenk tube was charged with charged with  $\text{Pd}(\text{CH}_3\text{CO}_2)_2$  (5.6 mg, 0.025 mmol), 1,3-bis(2,4,6-trimethylphenyl)imidazolinium chloride (10 mg, 0.025 mmol; Run a) or the bis(imidazolinium) dichloride shown in Run F of Table 6 (16 mg, 0.025 mmol; Runs b-h),  $\text{Cs}_2\text{CO}_3$  (652 mg, 2.00 mmol), and a magnetic stirring bar. After a 30 minute catalyst activation period, 1,4-dioxane (3 mL), aryl chloride (1.0 mmol), and arylboronic acid (1.5 mmol) were added in turn to the Schlenk tube. The Schlenk tube was placed in a 80°C oil bath and stirred for a number of hours. The mixture was then allowed to cool to room temperature. The aryl chlorides and arylboronic acids used in each run are listed in Table 7, along with the reaction times and isolated yields of the heterocoupling product.

TABLE 7

Run	Aryl chloride	Arylboronic acid	Reaction time	Isolated yield
a	4-Chlorotoluene	2-Methylphenylboronic acid	4 hr.	60%
b	4-Chlorotoluene	2-Methylphenylboronic acid	4 hr.	99%
c	4-Chlorotoluene	Phenylboronic acid	1.5 hr.	99%
d	4-Chlorotoluene	4-Methylphenylboronic acid	4 hr.	99%
e	1,4-Dimethyl-2-chlorobenzene	Phenylboronic acid	4 hr.	84%
f	Methyl-4-chlorobenzoate	Phenylboronic acid	2 hr.	99%
g	1-Me-3-ethylate-4-(4-Clphenyl)piperidine	Phenylboronic acid	4 hr.	96%
h	1-Me-4-cyano-4-(4-Clphenyl)piperidine	Phenylboronic acid	4 hr.	91%

Amine as Transmetalating Agent

The liquid medium for the processes of this invention can include any of a wide range of solvents, and mixtures of solvents are also usable. The exclusion of water is not necessary,

but is preferred. Types of solvents that can be used include hydrocarbons, ethers, amides, ketones, and alcohols. Polar solvents are preferred; ethers are a preferred solvent type. Ethers that may be used include, for example, diethyl ether, di-*n*-propyl ether, diisopropyl ether, *tert*-butyl ethyl ether, diheptyl ether, 1,3-dioxolane, 1,4-dioxane, tetrahydrofuran, methyl tetrahydrofuran, glyme (the dimethyl ether of ethylene glycol), diglyme (the dimethyl ether of diethylene glycol), and the like. Cyclic ethers and polyethers are preferred; a highly preferred ether is 1,4-dioxane.

A large variety of strong bases are suitable for use in the processes of this invention. Generally, these are inorganic bases. Alkali metal salts are a preferred group of inorganic bases. Examples of suitable alkali metal salts include, but are not limited to, lithium carbonate, lithium *tert*-butoxide, sodium acetate, sodium bicarbonate, sodium *tert*-butoxide, sodium oxide, sodium tetrafluoroborate, potassium acetate, potassium carbonate, potassium *tert*-butoxide, potassium nitrite, potassium phosphate, potassium sulfite, potassium hexafluorophosphate, cesium acetate, cesium bicarbonate, cesium carbonate, cesium fluoride, cesium nitrate, and cesium sulfate. Alkali metal salts of carboxylic acid anions (*e.g.*, acetate, trifluoroacetate, citrate, formate, oxalate, propionate, tartrate, *etc.*) are also suitable for use as the inorganic base in this invention. More preferred are salts of potassium and cesium; most preferred are potassium salts. The most highly preferred inorganic base is potassium *tert*-butoxide. Choice(s) of inorganic base will vary with the particular system of aryl halide or pseudohalide and amine involved.

Directly bonded to the aromatic ring(s) of the aryl halide or pseudohalide (*i.e.*, aryl halide or aryl pseudohalide) is at least one halogen atom selected from a chlorine atom, a bromine atom, and an iodine atom, or at least one pseudohalide group. The term "pseudohalide group" includes such groups as *p*-toluenesulfonate (tosylate), trifluoromethanesulfonate (triflate), methanesulfonate (meslyate), nonaflate (ON<sub>F</sub>), and aryl diazonium salts (ArN<sub>2</sub><sup>+</sup>X<sup>⊖</sup>, where X<sup>⊖</sup> is halide, BF<sub>4</sub><sup>⊖</sup>, *etc.*). The aryl halide or pseudohalide can have two or more such halogen atoms with an atomic number greater than nine and/or pseudohalide groups, including combinations of halogen atoms and pseudohalide groups. However, when two or more such groups are present, the halogen atoms with an atomic number greater than nine and/or pseudohalide groups should all be different from each other. For example, when two such substituents are present, they may be a chlorine atom and a

bromine atom, or an iodine atom and a tosylate group, or *etc.* It is preferred that there is only one chlorine atom, bromine atom, iodine atom, or pseudohalide group directly bound to the aryl ring of the aryl halide or pseudohalide. Aryl chlorides are more preferred as the aryl halide reactants. To prevent self-reaction, it is preferred that amino groups are not present on the aryl halide or pseudohalide.

The aryl moiety for the aryl halide or pseudohalide can be homocyclic or heterocyclic. Examples of suitable homocyclic aryl moieties include, but are not limited to, benzene, naphthalene, anthracene, phenanthrene, pyrene, biphenyl, acenaphthalene, fluorene, and indene. Heterocyclic aryl moieties that can be used include, for example, furan, thiophene, oxathiolane, thianthrene, isobenzofuran, phenoxathiin, and the like. Nitrogen-containing heterocycles, that can be used include, for example, pyridine, indole, isoxazole, and the like.. Benzene is a preferred aryl moiety for the aryl halide or pseudohalide.

For the aryl halide or pseudohalide, substituents other than a chlorine atom, a bromine atom, an iodine atom, and/or a pseudohalide group that may be present on the aromatic ring(s) include, but are not limited to, hydrogen atoms, fluorine atoms, nitro groups, hydrocarbyl groups, alkoxy groups, perfluorohydrocarbyl groups, silyl groups, amide groups, nitrile groups, ether groups, ketone groups, and ester groups. When hydrocarbyl groups are present, they are preferably C<sub>1</sub> to C<sub>18</sub> alkyl groups or C<sub>6</sub> to C<sub>20</sub> aryl or arylalkyl groups. Examples of suitable hydrocarbyl groups are methyl, ethyl, isopropyl, *tert*-butyl, cyclopentyl, methylcyclohexyl, decyl, phenyl, tolyl, xylyl, benzyl, naphthyl, and tetrahydronaphthyl. Alkoxy group substituents preferably have C<sub>1</sub> to C<sub>6</sub> alkyl moieties. Some examples of alkoxy groups are methoxy, ethoxy, isopropoxy, methylcyclopentoxy, and cyclohexoxy. Perfluorohydrocarbyl groups include alkyl and aryl perfluorocarbons; suitable perfluorohydrocarbyl groups are, for example, trifluoromethyl, pentafluoroethyl, pentafluorophenyl, and heptafluoronaphthyl. Substituent silyl groups preferably have C<sub>1</sub> to C<sub>18</sub> alkyl groups or C<sub>6</sub> to C<sub>20</sub> aryl or aralkyl groups, and examples include trimethylsilyl, triisopropylsilyl, *tert*-butyl(dimethyl)silyl, tridecylsilyl, and triphenylsilyl. The substituents preferred for the aryl halide or pseudohalide will depend on the product that is desired.

Amines suitable for use in this invention include primary and secondary amines. The group(s) of the amine may be saturated, unsaturated, branched, straight-chain, cyclic, or aromatic. Heteroatoms, such as oxygen, sulfur, and silicon, and/or functional groups

including ethers, esters, and ketones can be present in the group(s) of the amine. For secondary amines, the two groups on a particular amine may be the same or different.

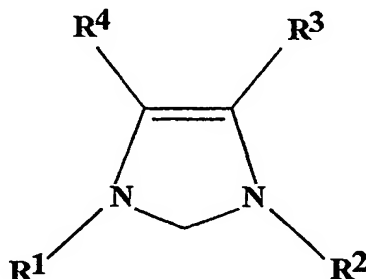
When an aryl moiety is present in the amine, the aryl moiety can be homocyclic or heterocyclic, as described for the aryl halide or pseudohalide. For the amine, the preferred aryl moieties are benzene and naphthalene. Substituents on the aryl ring, again as described for the aryl halide or pseudohalide, can be hydrogen atoms, fluorine atoms, nitro groups, hydrocarbyl groups, alkoxy groups, perfluorohydrocarbyl groups, silyl groups, ether groups, ketone groups, and ester groups. To prevent self-reaction, it is also preferred that chlorine atoms, bromine atoms, iodine atoms, and/or pseudohalide groups are not present on aromatic ring(s) in the amine. In other words, the aromatic rings in the amine are preferably devoid of halogen atoms with an atomic number greater than nine, and are preferably also devoid of pseudohalide groups. However, one or more fluorine atoms can be present on the aromatic ring(s).

Examples of primary amines include, but are not limited to, methylamine, cyclopropylamine, *n*-butylamine, *tert*-butylamine, cyclobutylamine, 2-pentylamine, hexylamine, heptylamine, octylamine, 4-methylcyclooctylamine, decylamine, phenylamine (aniline), 2,4,6-trimethylphenylamine (2,4,6-trimethylaniline), and benzylamine. Suitable secondary amines include dimethylamine, ethylmethylamine, diisopropylamine, di-*n*-butylamine, di-*sec*-butylamine, dicyclopentylamine, dihexylamine, di(methylcyclohexyl)amine, piperidine, morpholine, (ethyl)(octyl)amine, (nonyl)(*n*-propyl)amine, didodecylamine, N-methylphenylamine (N-methylaniline), (methyl)phenylamine, and the like. Primary or secondary amines may be preferred, depending on the product desired; similarly, preferred groups for the amine also depend on the desired product.

The metal compound comprises at least one metal atom selected from nickel, palladium, and platinum having a formal oxidation state of zero or two, and is sometimes referred to hereinafter as the metal compound. Inorganic salts of nickel, palladium, or platinum that can be used include the bromides, chlorides, fluorides, iodides, cyanides, nitrates, sulfides, sulfites, and sulfates. Organic nickel, palladium, or platinum compounds that may be used include complexes and salts such as the carboxylates, *e.g.*, the acetates or propionates, *etc.* Suitable nickel compounds include bis(1,5-cyclooctadiene)nickel, nickel

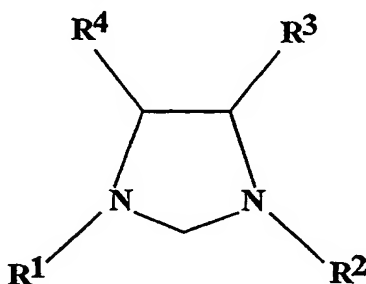
acetate, nickel oxalate, nickel phosphate, nickel stearate, nickel acetylacetonate, nickel tetrafluoroborate, nickel thiocyanate, nickel carbonate, and nickel sulfamate. Examples of palladium compounds include  $\text{Pd}(\text{OAc})_2$ , palladium(II) chloride,  $\text{Pd}(\text{CH}_3\text{CN})_4(\text{BF}_4)_2$ ,  $\text{PdCl}_2(\text{CH}_3\text{CN})_2$ ,  $\text{PdCl}_2(\text{PhCN})_2$ ,  $\text{PdCl}_2(\text{PPh}_3)_2$ , tris(dibenzylideneacetone)dipalladium(0) [which is also referred to herein as dipalladium tris(dibenzylideneacetone)], and palladium trifluoroacetate. Platinum compounds that can be used include platinum acetylacetonate and platinum chloride. Nickel and palladium compounds are preferred; more preferred are compounds of palladium. Palladium compounds such as palladium acetate and tris(dibenzylideneacetone)dipalladium(0) are most preferred.

Preferred types of N-heterocyclic carbenes are imidazoline-2-ylidenes of the formula



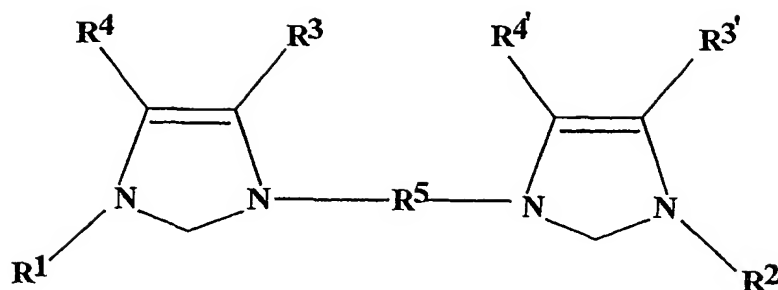
or protonated salts thereof, wherein  $\text{R}^1$  and  $\text{R}^2$  are each, independently, alkyl or aryl groups having at least 3 carbon atoms,  $\text{R}^3$  and  $\text{R}^4$  are each, independently, a hydrogen atom, a halogen atom, or a hydrocarbyl group;

imidazolidine-2-ylidenes of the formula



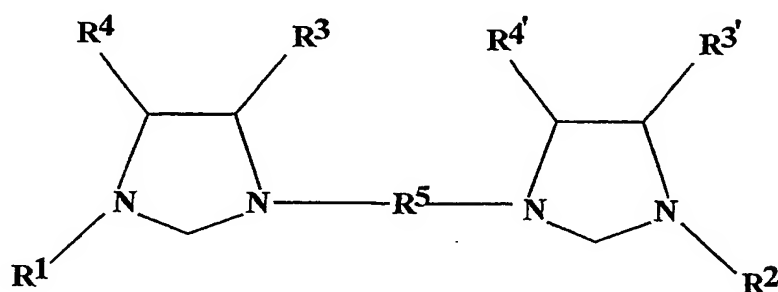
or protonated salts thereof, wherein  $\text{R}^1$ ,  $\text{R}^2$ ,  $\text{R}^3$ , and  $\text{R}^4$  are as defined for the imidazoline-2-ylidenes;

bis(imidazoline-2-ylidene)s of the formula



or protonated salts thereof, wherein  $R^1$ ,  $R^2$ ,  $R^3$ , and  $R^4$  are as defined for the imidazoline-2-ylidenes, wherein  $R^{3'}$  and  $R^{4'}$  are as defined for  $R^3$  and  $R^4$  for the imidazoline-2-ylidenes, and wherein  $R^5$  is a bridging group that links the two imidazoline rings;

bis(imidazolidine-2-ylidene)s of the formula



or protonated salts thereof, wherein  $R^1$ ,  $R^2$ ,  $R^3$ , and  $R^4$  are as defined for the imidazoline-2-ylidenes, wherein  $R^{3'}$  and  $R^{4'}$  are as defined for  $R^3$  and  $R^4$  for the imidazoline-2-ylidenes, and wherein  $R^5$  is a bridging group that links the two imidazolidine rings.

$R^1$  and  $R^2$  are preferably sterically bulky groups. Suitable groups include, but are not limited to, isopropyl, *sec*-butyl, *tert*-butyl, 2,2-dimethylpropyl (neopentyl), cyclohexyl, norbornyl, adamantyl, tolyl, 3,5-dimethylphenyl, 2,4,6-trimethylphenyl, 2,6-diisopropylphenyl, and triphenylmethyl. Preferred groups are *tert*-butyl, 2,4,6-trimethylphenyl, 2,6-diisopropylphenyl, 2,4,6-triisopropylphenyl, 2,4,6-triisopropylphenylmethyl, and triphenylmethyl. Most preferred for both  $R^1$  and  $R^2$  are the 2,4,6-trimethylphenyl, 2,6-diisopropylphenyl, and 2,4,6-triisopropylphenyl groups.

Examples of suitable  $R^3$ ,  $R^4$ ,  $R^{3'}$ , and  $R^{4'}$  groups include chlorine atoms, bromine atoms, hydrogen atoms, hydrocarbyl groups, and the like. When hydrocarbyl groups are present, they are preferably  $C_1$  to  $C_{18}$  alkyl groups or  $C_6$  to  $C_{20}$  aryl or aralkyl groups. Examples of suitable hydrocarbyl groups are methyl, ethyl, isopropyl, *tert*-butyl, cyclopentyl, methylcyclohexyl, decyl, phenyl, tolyl, xylyl, benzyl, naphthyl, and tetrahydronaphthyl. Chlorine atoms and hydrogen atoms are preferred groups. Most preferred for all substituents  $R^3$ ,  $R^4$ ,  $R^{3'}$ , and  $R^{4'}$  are hydrogen atoms.

$R^5$  in both the formula for the bis(imidazoline-2-ylidene)s and the bis(imidazolidine-2-ylidene)s of this invention can be selected from a large variety of moieties, including alkylene groups, arylene groups, and silylene groups. Atoms that can form the bridge include, but are not limited to, carbon, nitrogen, oxygen, silicon, and sulfur. Examples of suitable bridging moieties include methylene ( $-CH_2-$ ), substituted methylene, ethylene ( $-CH_2CH_2-$ ), substituted ethylene, silylene ( $>SiR_2$ ), benzo ( $C_6H_4<$ ), substituted benzo, biphenylene, substituted biphenylene, binaphthylene, and substituted binaphthylene. Heterocyclic aromatic moieties such as, for example, pyridine, pyrimidine, pyrazine, pyridazine, furan, thiophene, oxathiolane, thianthrene, isobenzofuran, phenoxathiin, isothiazole, phenoxazine, and the like, can also form the bridge. Preferred  $R^5$  moieties include biphenylene, binaphthylene, and substituted benzo, with substituted benzo being more preferred. Highly preferred is benzo substituted with methyl groups. The bridge has at least one atom, and more preferably has from four to eight atoms. While better results have been observed with longer bridges, it is possible that judicious choices for  $R^1$ ,  $R^2$ ,  $R^3$ ,  $R^4$ ,  $R^{3'}$ , and  $R^{4'}$  may improve results for short bridges.

Without being bound by theory, it appears from thermochemical studies that the electron-donating ability of many of the imidazoline-2-ylidene carbene ligands is better than that of tri(cyclohexyl)phosphine and the steric demand of these carbene ligands is greater than that of tri(cyclohexyl)phosphine. This suggests that the N-heterocyclic carbene should possess steric bulk sufficient to stabilize both the free carbene and to stabilize reaction intermediates. However, imidazoline-2-ylidene carbenes and imidazolidine-2-ylidene carbenes are considerably less stable to air and moisture than their corresponding protonated imidazolinium and imidazolidinium salts. Thus, a highly preferred embodiment of this



invention involves generation of the imidazoline-2-ylidene *in situ* from the corresponding imidazolinium salt (similarly so for the imidazolidine-2-ylidene and the corresponding imidazolidinium salt); this removes the need to handle the N-heterocyclic carbene ligands in an inert atmosphere. Protonated salts of the imidazoline-2-ylidene carbenes and imidazolidine-2-ylidene carbenes are monoprotonated, while the protonated salts of the bis(imidazoline-2-ylidene)s and the bis(imidazolidine-2-ylidene)s are diprotonated. Suitable counterions for the protonated salts are virtually limitless, but halides are preferred counterions. The most preferred counterions are chloride and bromide. The imidazolinium salts are straightforward to synthesize and are air-stable. While the absence of oxygen is not necessary when using a protonated salt of an imidazoline-2-ylidene carbene or an imidazolidine-2-ylidene carbene, it is preferred. When using a neutral carbene, the absence of oxygen is necessary. In any instance where oxygen is excluded, the presence of an inert gas such as nitrogen, helium, or argon is preferred.

The aryl halide or pseudohalide and the amine may be employed in an ideal molar ratio of about 1:1 when using an aryl halide or pseudohalide that has only one halogen atom (other than a fluorine atom) or pseudohalide group; or either reagent may be used in excess. It is preferred to use the amine in an excess such that the molar ratio of aryl halide or pseudohalide to amine is in the range of from about 1:1 to about 1:3 when using an aryl halide or pseudohalide that has only one halogen atom (other than a fluorine atom) or pseudohalide group. When the aryl halide or pseudohalide has more than one halogen atom (other than fluorine) and/or pseudohalide group, reactions may be carried out in sequence. An amine will react first at the site of the more reactive substituent, *e.g.*, at iodine before bromine. Reaction at only the site of the more reactive substituent(s) can be performed. In reactions carried out in sequence where the amines are different, each should be added separately. It is preferred to allow one reaction to finish before the addition of the next amine. When different amines are used, it is preferred to use close to the ideal molar ratio of aryl halide or pseudohalide to amine to minimize undesirable side products.

A suitable molar ratio of aryl halide or pseudohalide to strong base is in the range of from about 1:1 to about 1:5. A more preferred molar ratio of aryl halide or pseudohalide to strong base is in the range of from about 1:1 to about 1:3.

Normally, the molar ratio of metal atoms of the metal compound to aryl halide or

pseudohalide molecules is in the range of from about 0.01:1 to about 0.05:1; a preferred molar ratio of metal atoms of metal compound to aryl halide or pseudohalide molecules is in the range of from about 0.01:1 to about 0.03:1. For the metal compound and the carbene ligands, the molar ratio of metal atoms of the metal compound to carbene molecules is in the range of from about 1:0.5 to about 1:5, and more preferably in the range of from about 1:1 to about 1:3.

The order of addition of the various components to a reaction vessel is not of particular importance. Premixing of the components of the catalyst system is not necessary; however, it is preferred that the catalyst system is premixed. To premix the components of the catalyst system, the metal compound and the N-heterocyclic carbene (salt or neutral compound) are mixed together after being added in no particular order to a reaction vessel. The mixing time (activation period) for these components on the laboratory scale may be very short, *e.g.*, five minutes or less, but a preferred mixing time is in the range of from about fifteen minutes to about sixty minutes.

If a premixed catalyst system is used, the aryl halide or pseudohalide, the amine, and the strong base may be added to the same reaction vessel, or the premixed catalyst system can be transferred to a different vessel in which the reaction is to take place. Use of the same vessel for premixing the catalyst system and conducting the reaction is preferred.

When the components of the catalyst system are not premixed, the strong base, aryl halide or pseudohalide, the amine, the metal compound, the liquid medium, and the N-heterocyclic carbene (salt or neutral compound) are added in any order to the reaction vessel.

Once all of the components are present in the same reaction vessel, the mixture may be heated, provided that the temperature does not exceed the thermal decomposition temperature of the catalyst system or the products of the reaction. Preferred temperatures are in the range of from about 20°C to about 150°C; more preferred temperatures are in the range of from about 20°C to about 120°C. When the aryl halide or pseudohalide is an aryl chloride, an aryl triflate, an aryl tosylate, aryl mesylate, aryl trifluoromethanesulfone, aryl nonaflate, or aryl diazonium salt, heat is usually necessary to drive the reaction. Preferred temperatures when the aryl halide or pseudohalide is an aryl chloride, an aryl triflate, or an aryl tosylate are in the range of from about 40°C to about 150°C. When the aryl halide or pseudohalide is an aryl bromide or an aryl iodide, the reaction(s) proceeds easily at room temperature, although

heat may speed the reaction. For aryl bromides and aryl iodides, preferred temperatures are in the range of from about 20°C to about 70°C.

While not necessary when using protonated salts of N-heterocyclic carbenes, the absence of oxygen and water is preferred when conducting the processes of this invention. Conversely, the exclusion of oxygen and water is generally necessary when neutral carbenes are used. The presence of an inert gas such as argon or nitrogen is preferred when oxygen and/or water are excluded. The reaction mixture is normally agitated. A preferred contact time for the components of the reaction is in the range of from about one hour to about seventy-two hours. More preferably, the contact time is from about one hour to about forty-eight hours.

The following examples are presented for purposes of illustration, and are not intended to impose limitations on the scope of this embodiment of the invention.

## EXAMPLES 9-12

### GENERAL PROCEDURES

**Reagents.** All aryl halides (Aldrich Chemical Company), amines (Aldrich), 1,4-dioxane (anhydrous, Aldrich), KO<sup>t</sup>Bu (Aldrich), and Pd<sub>2</sub>(dibenzylideneacetone)<sub>3</sub> (Strem Chemical Company) were used as received. Flash chromatography was performed on silica gel 60 (230-400 mesh; Natland International Corporation).

1,3-Bis(substituted)imidazoline-2-ylidenes and 1,3-bis(substituted)imidazolinium chlorides were prepared according to reported procedures in U.S. Patent No. 5,077,414, and/or Arduengo, A. J. III., Dias, H.V.R.; Harlow, R.L. and Kline, M. *J. Am. Chem. Soc.*, 1992, 114, 5530-5534. The synthesis of 1,3-bis(2,6-diisopropylphenyl)imidazolinium chloride was carried out in a similar fashion, except that it was done in two steps (rather than in one pot).

**Analyses.** All reactions were monitored by thin layer chromatography (TLC). <sup>1</sup>H and <sup>13</sup>C nuclear magnetic resonance (NMR) spectra were recorded on a 300 MHz NMR spectrometer (Varian, Incorporated) or 400 MHz NMR spectrometer (Varian) at ambient temperature in CDCl<sub>3</sub> (Cambridge Isotope Laboratories, Incorporated). All of the products had <sup>1</sup>H NMR spectra identical with literature data.

**Conditions.** All reactions were carried out under an atmosphere of argon in oven-dried glassware with magnetic stirring, unless otherwise indicated.

**EXAMPLE 9**

For each run, a Schlenk tube was charged with  $\text{Pd}_2(\text{dibenzylideneacetone})_3$  (10 mg, 0.01 mmol), 1,3-bis(substituted)imidazolinium chloride (0.04 mmol), and a magnetic stirring bar. After a 30 minute catalyst activation period, 1,4-dioxane (3 mL),  $\text{KO}^t\text{Bu}$  (168mg, 1.5 mmol), 4-chlorotoluene (1.0 mmol), and N-methylaniline (1.2 mmol) were added in turn to the Schlenk tube. The Schlenk tube was placed in a 100°C oil bath and the mixture was stirred for 3 hours. The mixture was then allowed to cool to room temperature. The mixture was washed with diethyl ether. The organic layer and the diethyl ether extracts were combined, washed with saturated saline solution, and then dried over  $\text{MgSO}_4$ . The solvent was removed under vacuum and the residue was purified by flash chromatography using hexane or a mixture of hexane and ethyl acetate.

The 1,3-bis(substituted)imidazolinium chloride used in each run are listed in Table 8. All of the yields reported in Table 8 are of the heterocoupling product, and are the average of two runs.

**TABLE 8**

Run	1,3-Bis(substituted)imidazolinium chloride	Isolated yield
a	None	0
b	1,3-Bis( <i>p</i> -tolyl)imidazolinium chloride	<5%
c	1,3-Bis(2,6-dimethylphenyl)imidazolinium chloride	11%
d	1,3-Bis(2,4,6-trimethylphenyl)imidazolinium chloride	22%
e	1,3-Bis(2,6-diisopropylphenyl)imidazolinium chloride	98%

**EXAMPLE 10**

Reagents, analyses, and procedures were as described in Example 9, except as follows. The 1,3-bis(substituted)imidazolinium chloride used in all runs was 1,3-Bis(2,6-diisopropylphenyl)imidazolinium chloride. Several different aryl chlorides (1.0 mmol each) and amines (1.2 mmol each) were used. Reactions were complete in three to thirty hours, but reaction times have not been optimized.

The aryl chlorides and amines used in each run are listed in Table 9;. All of the yields reported in Table 9 are of the heterocoupling product, and are the average of two runs.

TABLE 9

Run	Aryl chloride	Amine	Isolated yield
a	4-Chlorotoluene	N-Methylaniline	99%
b	4-Chlorotoluene	Piperidine	96%
c	4-Chlorotoluene	Morpholine	82%
d	4-Chlorotoluene	Di- <i>n</i> -butylamine	95%
e	4-Chlorotoluene	Hexylamine	86% <sup>a</sup>
f	4-Chlorotoluene	Aniline	96%
g	4-Chlorotoluene	2,4,6-Trimethylaniline	59%
h	1-Methoxy-4-chlorobenzene	Methylaniline	91%
i	1-Methoxy-4-chlorobenzene	Aniline	91%
j	1-Methoxy-4-chlorobenzene	Morpholine	80%
k	1-Methoxy-4-chlorobenzene	Di- <i>n</i> -butylamine	98%
l	1,4-Dimethyl-2-chlorobenzene	N-Methylaniline	94%

<sup>a</sup>A 5% yield of dihexylaniline was also obtained.

## EXAMPLE 11

Reagents, analyses, and procedures were as described in Example 9, except as follows. The 1,3-bis(substituted)imidazolinium chloride used in all runs was 1,3-Bis(2,6-diisopropylphenyl)imidazolinium chloride. Several different aryl halides (1.0 mmol each) and amines (1.2 mmol each) were used. Reactions were complete in three to thirty hours, but reaction times have not been optimized.

The aryl halides and amines used in each run are listed in Table 10. All of the yields reported in Table 10 are of the heterocoupling product, and are the average of two runs.

TABLE 10

Run	Aryl halide	Amine	Isolated yield
a	4-Bromotoluene	Methylaniline	89%
b	4-Bromotoluene	Piperidine	83%
c	1-Bromo-4-chlorobenzene	Piperidine	94%
d	1-Chloro-4-iodobenzene	Piperidine	97%

## EXAMPLE 12

Reagents, analyses, and procedures were as described in Example 9, except as follows. In all runs, the 1,3-bis(substituted)imidazolinium chloride used was 1,3-Bis(2,6-diisopropylphenyl)imidazolinium chloride (0.02 mmol); the metal compound was Pd(dibenzylideneacetone)<sub>2</sub> (0.02 mmol); the amine was aniline; and the reaction time was 48 hours. Several different aryl pseudohalides (1.0 mmol each) were used.

The aryl pseudohalides used in each run are listed in Table 11. All yields reported in Table 11 are of the heterocoupling product, and are the average of two runs.

TABLE 11

Run	Aryl pseudohalide	Isolated yield
a	1-Methyl-4-(triflate)benzene	<5%
b	1-Methoxy-4-(triflate)benzene	30%
c	Methyl-4-(triflate)benzoate	22%
d	1-Methyl-4-(tosylate)benzene	NR <sup>a</sup>

<sup>a</sup>NR = no reaction

Grignard as Transmetalating Agent

As noted above, there are two fundamental aspects to this invention. One aspect is the provision of exceedingly efficient catalyzed Kumada coupling reactions. The other aspect involves the discovery of catalyzed homocoupling reactions in which aryl triflates or aryl tosylates are caused to homocouple even in the presence of a Grignard reagent.

The liquid medium for the processes of this invention can include any of a wide range of solvents, and mixtures of solvents are also usable. The exclusion of water is necessary because the processes of this invention use Grignard reagents. Of course, "exclusion of water" as used here is intended to mean that no addition of water should be undertaken and that necessary steps should be taken to avoid unintended introduction of water into the reaction. However, inconsequential amounts of water which have no meaningful effect upon the reaction may be present. Thus, the reaction is carried out in the substantial absence of water. Types of solvents that can be used include hydrocarbons, ethers, and amides. Polar solvents are preferred. When a hydrocarbon solvent is included in the liquid medium, it is preferred that the hydrocarbon solvent makes up less than a third (by volume) of the liquid

medium. Ethers are a preferred solvent type. Ethers that may be used include, for example, diethyl ether, di-*n*-propyl ether, diisopropyl ether, *tert*-butyl ethyl ether, diheptyl ether, 1,3-dioxolane, 1,4-dioxane, tetrahydrofuran, methyl tetrahydrofuran, glyme (the dimethyl ether of ethylene glycol), diglyme (the dimethyl ether of diethylene glycol), and the like. Cyclic ethers and polyethers are preferred, especially 1,4-dioxane and tetrahydrofuran. Mixtures comprising tetrahydro-furan are more preferred; a highly preferred liquid medium is a mixture of 1,4-dioxane and tetrahydrofuran.

Directly bonded to the aromatic ring(s) of the aryl halide or pseudohalide (i.e., aryl halide or aryl pseudohalide) is at least one halogen atom selected from a chlorine atom, a bromine atom, and an iodine atom, or at least one pseudohalide group. The term "pseudohalide group" includes such groups as *p*-toluene sulfonate (tosylate), trifluoromethanesulfonate (triflate), methanesulfonate (meslyate), nonaflate ( $\text{ON}_f$ ), and aryl diazonium salts ( $\text{ArN}_2^+\text{X}^-$ , where  $\text{X}^-$  is halide,  $\text{BF}_4^-$ , etc.). The aryl halide or pseudohalide can have two or more such halogen atoms with an atomic number greater than nine and/or pseudohalide groups, including combinations of halogen atoms and pseudohalide groups. However, when two or more such groups are present, the halogen atoms with an atomic number greater than nine and/or pseudohalide groups should all be different from each other. For example, when two such substituents are present, they may be a chlorine atom and a bromine atom, or an iodine atom and a tosylate group, or *etc.* It is preferred that there is only one chlorine atom, bromine atom, iodine atom, or pseudohalide group directly bound to the aryl ring of the aryl halide or pseudohalide. Aryl chlorides are more preferred as the aryl halide reactants.

The aryl moiety for the aryl halide or pseudohalide can be homocyclic or heterocyclic. Examples of suitable homocyclic aryl moieties include, but are not limited to, benzene, naphthalene, anthracene, phenanthrene, pyrene, biphenyl, acenaphthalene, fluorene, and indene. Heterocyclic aryl moieties that can be used include, for example, furan, thiophene, pyridine, indole, oxathiolane, isoxazole, thianthrene, isobenzofuran, phenoxathiin, and the like. Benzene is a preferred aryl moiety for the aryl halide or pseudohalide.

For the aryl halide or pseudohalide, substituents other than a chlorine atom, a bromine atom, an iodine atom, and/or a pseudohalide group that may be present on the aromatic ring(s) include, but are not limited to, hydrogen atoms, fluorine atoms, nitro groups, hydrocarbyl

groups, alkoxy groups, perfluorohydrocarbyl groups, silyl groups, amino groups, ether groups, ketone groups, and ester groups. When hydrocarbyl groups are present, they are preferably  $C_1$  to  $C_{18}$  alkyl groups or  $C_6$  to  $C_{20}$  aryl or aralkyl groups. Examples of suitable hydrocarbyl groups are methyl, ethyl, isopropyl, *tert*-butyl, cyclopentyl, methylcyclohexyl, decyl, phenyl, tolyl, xylyl, benzyl, naphthyl, and tetrahydronaphthyl. Alkoxy group substituents preferably have  $C_1$  to  $C_6$  alkyl moieties. Some examples of alkoxy groups are methoxy, ethoxy, isopropoxy, methylcyclopentoxy, and cyclohexoxy. Perfluorohydrocarbyl groups include alkyl and aryl perfluorocarbons; suitable perfluorohydrocarbyl groups are, for example, trifluoromethyl, pentafluoroethyl, pentafluorophenyl, and heptafluoronaphthyl. Substituent silyl groups preferably have  $C_1$  to  $C_{18}$  alkyl groups or  $C_6$  to  $C_{20}$  aryl or aralkyl groups, and examples include trimethylsilyl, triisopropylsilyl, *tert*-butyl(dimethyl)silyl, tridecylsilyl, and triphenylsilyl. The substituents preferred for the aryl halide or pseudohalide will depend on the product that is desired.

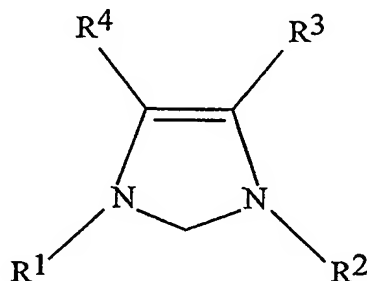
The Grignard reagent can be an organomagnesium chloride, an organomagnesium bromide, or an organomagnesium iodide, and is preferably an organomagnesium bromide. The organic group of the Grignard reagent may be saturated, unsaturated, branched, straight-chain, cyclic, or aromatic. Heteroatoms, such as oxygen, sulfur, and silicon can be present in the organic group of the Grignard reagent. The organic group of the Grignard reagent is preferably an aromatic group. The aryl moiety of the aromatic group can be homocyclic or heterocyclic, as described for the aryl halide or pseudohalide. For the Grignard reagent, the preferred aryl moieties are benzene and naphthalene. Substituents on the aryl ring, as described for the aryl halide or pseudohalide, can be hydrogen atoms, fluorine atoms, nitro groups, hydrocarbyl groups, alkoxy groups, perfluorohydrocarbyl groups, and silyl groups. Preferred substituents for the Grignard reagent depend on the desired product.

The metal compound comprises at least one metal atom selected from nickel, palladium, and platinum having a formal oxidation state of zero or two, and is sometimes referred to hereinafter as the metal compound. Inorganic salts of nickel, palladium, or platinum that can be used include the bromides, chlorides, fluorides, iodides, cyanides, nitrates, sulfides, sulfites, and sulfates. Organic nickel, palladium, or platinum compounds that may be used include complexes and salts such as the carboxylates, *e.g.*, the acetates or propionates, *etc.* Suitable nickel compounds include bis(1,5-cyclooctadiene)nickel, nickel



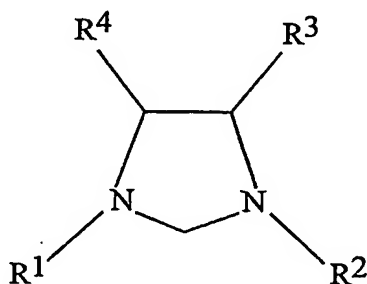
acetate, nickel oxalate, nickel phosphate, nickel stearate, nickel acetylacetonate, nickel tetrafluoroborate, nickel thiocyanate, nickel carbonate, and nickel sulfamate. Examples of palladium compounds include  $\text{Pd}(\text{OAc})_2$ , palladium(II) chloride,  $\text{Pd}(\text{CH}_3\text{CN})_4(\text{BF}_4)_2$ ,  $\text{PdCl}_2(\text{CH}_3\text{CN})_2$ ,  $\text{PdCl}_2(\text{PhCN})_2$ ,  $\text{PdCl}_2(\text{PPh}_3)_2$ , tris(dibenzylideneacetone)dipalladium(0) [which is also referred to herein as dipalladium tris(dibenzylideneacetone)], and palladium trifluoroacetate. Platinum compounds that can be used include platinum acetylacetonate and platinum chloride. Nickel and palladium compounds are preferred; more preferred are compounds of palladium. Palladium compounds such as palladium acetate and tris(dibenzylideneacetone)dipalladium(0) are most preferred.

Preferred types of N-heterocyclic carbenes are imidazoline-2-ylidenes of the formula



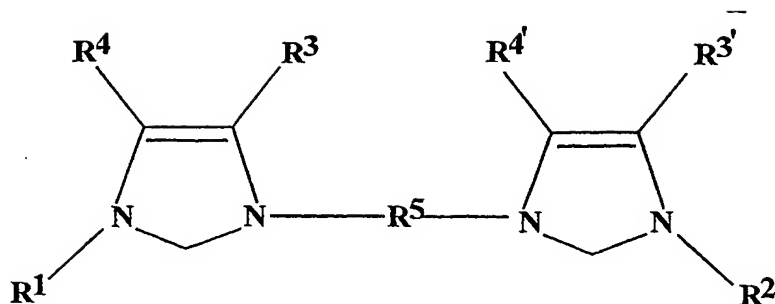
or protonated salts thereof, wherein  $\text{R}^1$  and  $\text{R}^2$  are each, independently, alkyl or aryl groups having at least 3 carbon atoms,  $\text{R}^3$  and  $\text{R}^4$  are each, independently, a hydrogen atom, a halogen atom, or a hydrocarbyl group;

imidazolidine-2-ylidenes of the formula



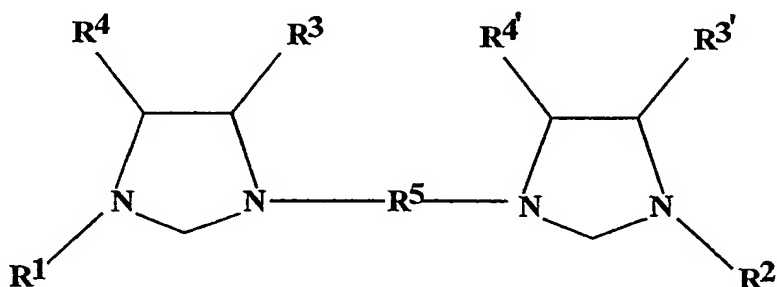
or protonated salts thereof, wherein  $\text{R}^1$ ,  $\text{R}^2$ ,  $\text{R}^3$ , and  $\text{R}^4$  are as defined for the imidazoline-2-ylidenes;

bis(imidazoline-2-ylidene)s of the formula



or protonated salts thereof, wherein  $R^1$ ,  $R^2$ ,  $R^3$ , and  $R^4$  are as defined for the imidazoline-2-ylidenes, wherein  $R^{3'}$  and  $R^{4'}$  are as defined for  $R^3$  and  $R^4$  for the imidazoline-2-ylidenes, and wherein  $R^5$  is a bridging group that links the two imidazoline rings;

bis(imidazolidine-2-ylidene)s of the formula



or protonated salts thereof, wherein  $R^1$ ,  $R^2$ ,  $R^3$ , and  $R^4$  are as defined for the imidazoline-2-ylidenes, wherein  $R^{3'}$  and  $R^{4'}$  are as defined for  $R^3$  and  $R^4$  for the imidazoline-2-ylidenes, and wherein  $R^5$  is a bridging group that links the two imidazolidine rings.

$R^1$  and  $R^2$  are preferably sterically bulky groups. Suitable groups include, but are not limited to, isopropyl, *sec*-butyl, *tert*-butyl, 2,2-dimethylpropyl (neopentyl), cyclohexyl, norbornyl, adamantyl, tolyl, 3,5-dimethylphenyl, 2,4,6-trimethylphenyl, 2,6-diisopropylphenyl, and triphenylmethyl. Preferred groups are *tert*-butyl, 2,4,6-trimethylphenyl, 2,6-diisopropylphenyl, 2,4,6-triisopropylphenyl, 2,4,6-triisopropylphenylmethyl and triphenylmethyl. Most preferred for both  $R^1$  and  $R^2$  are the 2,4,6-trimethylphenyl and 2,6-diisopropylphenyl groups.

Examples of suitable  $R^3$ ,  $R^4$ ,  $R^{3'}$ , and  $R^{4'}$  groups include chlorine atoms, bromine atoms, hydrogen atoms, hydrocarbyl groups, and the like. When hydrocarbyl groups are present, they are preferably  $C_1$  to  $C_{18}$  alkyl groups or  $C_6$  to  $C_{20}$  aryl or aralkyl groups. Examples of suitable hydrocarbyl groups are methyl, ethyl, isopropyl, *tert*-butyl, cyclopentyl, methylcyclohexyl, decyl, phenyl, tolyl, xylyl, benzyl, naphthyl, and tetrahydronaphthyl. Chlorine atoms and hydrogen atoms are preferred groups. Most preferred for all substituents  $R^3$ ,  $R^4$ ,  $R^{3'}$ , and  $R^{4'}$  are hydrogen atoms.

$R^5$  in both the formula for the bis(imidazoline-2-ylidene)s and the bis(imidazolidine-2-ylidene)s of this invention can be selected from a large variety of moieties, including alkylene groups, arylene groups, and silylene groups. Atoms that can form the bridge include, but are not limited to, carbon, nitrogen, oxygen, silicon, and sulfur. Examples of suitable bridging moieties include methylene ( $-\text{CH}_2-$ ), substituted methylene, ethylene ( $-\text{CH}_2\text{CH}_2-$ ), substituted ethylene, silylene ( $>\text{SiR}_2$ ), benzo ( $\text{C}_6\text{H}_4<$ ), substituted benzo, biphenylene, substituted biphenylene, binaphthylene, and substituted binaphthylene. Heterocyclic aromatic moieties such as, for example, pyridine, pyrimidine, pyrazine, pyridazine, furan, thiophene, oxathiolane, thianthrene, isobenzofuran, phenoxathiin, isothiazole, phenoxazine, and the like, can also form the bridge. Preferred  $R^5$  moieties include biphenylene, binaphthylene, and substituted benzo, with substituted benzo being more preferred. Highly preferred is benzo substituted with methyl groups. The bridge has at least one atom, and preferably has from four to eight atoms. While better results have been observed with longer bridges, it is possible that judicious choices for  $R^1$ ,  $R^2$ ,  $R^3$ ,  $R^4$ ,  $R^{3'}$ , and  $R^{4'}$  may improve results for short bridges.

Without being bound by theory, it appears from thermochemical studies that the electron-donating ability of many of the imidazoline-2-ylidene carbene ligands is better than that of tri(cyclohexyl)phosphine and the steric demand of these carbene ligands is greater than that of tri(cyclohexyl)phosphine. This suggests that the N-heterocyclic carbene should possess steric bulk sufficient to stabilize both the free carbene and to stabilize reaction intermediates. However, imidazoline-2-ylidene carbenes and imidazolidine-2-ylidene carbenes are considerably less stable to air and moisture than their corresponding protonated imidazolinium and imidazolidinium salts. Thus, a highly preferred embodiment of this invention involves generation of the imidazoline-2-ylidene *in situ* from the corresponding

imidazolinium salt (similarly so for the imidazolidine-2-ylidene and the corresponding imidazolidinium salt); this removes the need to handle the N-heterocyclic carbene ligands in an inert atmosphere. Protonated salts of the imidazoline-2-ylidene carbenes and imidazolidine-2-ylidene carbenes are monoprotinated, while the protonated salts of the bis(imidazoline-2-ylidene)s and the bis(imidazolidine-2-ylidene)s are diprotinated. Suitable counterions for the protonated salts are virtually limitless, but halides are preferred counterions. The most preferred counterions are chloride and bromide. The imidazolinium salts are straightforward to synthesize and are air-stable. While the absence of oxygen is not necessary when using a protonated salt of an imidazoline-2-ylidene carbene or an imidazolidine-2-ylidene carbene, it is preferred. When using a neutral carbene, the absence of oxygen is necessary. In any instance where oxygen is excluded, the presence of an inert gas such as nitrogen, helium, or argon is preferred.

For the Kumada coupling reaction, the aryl halide or pseudohalide and the Grignard reagent may be employed in an ideal molar ratio of about 1:1 when using an aryl halide or pseudohalide that has only one halogen atom (other than a fluorine atom) or pseudohalide group; or either reagent may be used in excess. It is preferred to use the Grignard reagent in an excess such that the molar ratio of aryl halide or pseudohalide to Grignard reagent is in the range of from about 1:1 to about 1:5 when using an aryl halide or pseudohalide that has only one halogen atom (other than a fluorine atom) or pseudohalide group. When the aryl halide or pseudohalide has more than one halogen atom (other than fluorine) and/or pseudohalide group, reactions may be carried out in sequence. A Grignard reagent will react first at the site of the more reactive substituent, *e.g.*, at iodine before bromine. Reaction at only the site of the more reactive substituent(s) can be performed. In reactions carried out in sequence where the Grignard reagents are different, each should be added separately. It is preferred to allow one reaction to finish before the addition of the next Grignard reagent. When different Grignard reagents are used, it is preferred to use close to the ideal molar ratio of aryl halide or pseudohalide to Grignard reagent to minimize undesirable side products. The presence of a Grignard reagent is not necessary in a homocoupling reaction.

Normally, the molar ratio of metal atoms of the metal compound to aryl halide or pseudohalide molecules is in the range of from about 0.01:1 to about 0.05:1; a preferred molar ratio of metal atoms of metal compound to aryl halide or pseudohalide molecules is in the

range of from about 0.02:1 to about 0.04:1. For the metal compound and the carbene ligands, the molar ratio of metal atoms of the metal compound to carbene molecules is in the range of from about 1:0.5 to about 1:5, and more preferably in the range of from about 1:0.5 to about 1:2.5.

The order of addition of the various components to a reaction vessel is not of particular importance for either heterocoupling or homocoupling reactions. Premixing of the components of the catalyst system is not necessary; however, it is preferred for both heterocoupling and homocoupling reactions that the catalyst system is premixed. To premix the components of the catalyst system, the metal compound and the N-heterocyclic carbene (salt or neutral compound), are mixed together after being added in no particular order to a reaction vessel. The mixing time (activation period) for these components on the laboratory scale may be very short, *e.g.*, five minutes or less, but a preferred mixing time is in the range of from about fifteen minutes to about sixty minutes.

If a premixed catalyst system is used, the aryl halide or pseudohalide and the Grignard reagent may be added to the same reaction vessel, or the premixed catalyst system can be transferred to a different vessel in which the reaction is to take place. Use of the same vessel for premixing the catalyst system and conducting the reaction is preferred.

For both heterocoupling and homocoupling reactions, when the components of the catalyst system are not premixed, all of the components of the reaction mixture are added in any order to the reaction vessel.

Once all of the components are present in the same reaction vessel, the mixture may be heated, provided that the temperature does not exceed the thermal decomposition temperature of the catalyst system or the products of the reaction. Preferred temperatures for both heterocoupling and homocoupling reactions are in the range of from about 20°C to about 150°C; more preferred temperatures are in the range of from about 20°C to about 120°C. When the aryl halide is an aryl chloride, or when the aryl pseudohalide is an aryl triflate or an aryl tosylate, heat is usually necessary to drive the reaction. Preferred temperatures when the aryl halide is an aryl chloride, or when the aryl pseudohalide is an aryl triflate or an aryl tosylate are in the range of from about 40°C to about 150°C. When the aryl halide is an aryl bromide or an aryl iodide, the reaction(s) proceeds easily at room temperature, although heat may speed the reaction. For aryl bromides and aryl iodides, preferred temperatures are in the

range of from about 20°C to about 70°C.

When a Grignard reagent is used, the exclusion of water is generally required; thus, heterocoupling reactions are normally carried out in the absence of water. While not necessary when using protonated salts of N-heterocyclic carbenes, the absence of oxygen is preferred when conducting the processes of this invention. Conversely, the exclusion of oxygen and water is generally necessary when neutral carbenes are used. The presence of an inert gas such as argon or nitrogen is preferred when oxygen and/or water are excluded. The reaction mixture is normally agitated. A preferred contact time for the components of either a heterocoupling or a homocoupling reaction is in the range of from about one hour to about seventy-two hours. More preferably, the contact time is from about one hour to about forty-eight hours.

The following examples are presented for purposes of illustration, and are not intended to impose limitations on the scope of this embodiment of the invention.

### EXAMPLES 13-16

#### GENERAL PROCEDURES

**Reagents.** All aryl halides (Aldrich Chemical Company), arylmagnesium bromides (1.0 moles per liter in tetrahydrofuran; Aldrich), 1,4-dioxane (anhydrous, Aldrich), and  $\text{Pd}_2(\text{dibenzylideneacetone})_3$  (Strem Chemical Company) were used as received. Flash chromatography was performed on silica gel 60 (230-400 mesh; Natland International Corporation).

1,3-Bis(substituted)imidazoline-2-ylidenes and 1,3-bis(substituted)imidazolinium chlorides were prepared according to reported procedures in U.S. Patent No. 5,077,414, and/or Arduengo, A. J. III., Dias, H.V.R.; Harlow, R.L. and Kline, M. *J. Am. Chem. Soc.*, 1992, **114**, 5530-5534. The synthesis of 1,3-bis(2,6-diisopropylphenyl)imidazolinium chloride was carried out in a similar fashion, except that it was done in two steps (rather than in one pot).

**Analyses.** All reactions were monitored by thin layer chromatography (TLC).  $^1\text{H}$  and  $^{13}\text{C}$  nuclear magnetic resonance (NMR) spectra were recorded on a 300 MHz NMR spectrometer (Varian, Incorporated) or 400 MHz NMR spectrometer (Varian) at ambient temperature in  $\text{CDCl}_3$  (Cambridge Isotope Laboratories, Incorporated). All of the products had  $^1\text{H}$  NMR spectra identical with literature data.

**Conditions.** All reactions were carried out under an atmosphere of argon in oven-dried glassware with magnetic stirring, unless otherwise indicated.

### EXAMPLE 13

For each run, a Schlenk tube was charged with  $\text{Pd}_2(\text{dibenzylideneacetone})_3$  (10 mg, 0.01 mmol), 1,3-bis(substituted)imidazolinium chloride (0.04 mmol), and a magnetic stirring bar. After a 30 minute catalyst activation period, solvent (5 mL), 4-chlorotoluene (1.0 mmol), and phenylmagnesium bromide (1.2 mmol) were added in turn to the Schlenk tube. The Schlenk tube was placed in an oil bath and the mixture was heated and stirred for a number of hours. The mixture was then allowed to cool to room temperature. The mixture was hydrolyzed either with aqueous HCl (1.0 moles per liter) or  $\text{H}_4\text{NCl}$  solution. The solvent was removed under vacuum and the residue was purified by flash chromatography using hexane or a mixture of hexane and ethyl acetate.

The 1,3-bis(substituted)imidazolinium chloride used in each run are listed in Table 12. All of the yields reported in Table 12 are of the heterocoupling product, and are the average of two runs.

TABLE 12

Run	1,3-bis(substituted)imidazolinium chloride	Solvent	T	Reaction time	Isolated yield
a	1,3-Bis(2,4,6-trimethylphenyl)-imidazolinium chloride	$\text{Et}_2\text{O}/\text{THF}$	45°C	20 hr.	35%
b	1,3-Bis(2,6-diisopropylphenyl)-imidazolinium chloride	$\text{Et}_2\text{O}/\text{THF}$	45°C	20 hr.	97%
c	1,3-Bis(2,6-diisopropylphenyl)-imidazolinium chloride	toluene/THF	80°C	20 hr.	10%
d	1,3-Bis(2,6-diisopropylphenyl)-imidazolinium chloride	THF	80°C	5 hr.	86%
e	None	dioxane/THF	80°C	3 hr.	0
f	1,3-Bis(2,4,6-trimethylphenyl)-imidazolinium chloride	dioxane/THF	80°C	3 hr.	41%
g	1,3-Bis(2,6-diisopropylphenyl)-imidazolinium chloride	dioxane/THF	80°C	3 hr.	99%

## EXAMPLE 14

Reagents, analyses, and procedures were as described in Example 13, except as follows. In all runs, the solvent was a mixture of 1,4-dioxane and tetrahydrofuran; the 1,3-bis(substituted)imidazolinium chloride used was 1,3-bis(2,6-diisopropylphenyl)imidazolinium chloride. All runs were performed at 80°C. Several different aryl halides (1.0 mmol each) and Grignard reagents (1.2 mmol each) were used. In Run B,  $\text{Pd}(\text{CH}_3\text{CO}_2)_2$  (4.5mg, 0.02 mmol) was used as the metal compound; in Run F, 1.8 mmol of the Grignard reagent was used, and in Runs H and I, 2.5 mmol of the Grignard reagent was used.

The aryl halides and Grignard reagents used in each run are listed in Table 13. All of the yields reported in Table 13 are of the heterocoupling product, and are the average of two runs.

TABLE 13

Run	Aryl halide	Grignard reagent	Reaction time	Isolated yield
A	4-Chorotoluene	Phenylmagnesium bromide	3 hr.	99%
B	4-Chorotoluene	Phenylmagnesium bromide	3 hr.	96%
C	4-Bromotoluene	Phenylmagnesium bromide	1 hr.	99%
D	1-Methoxy-4-chlorobenzene	Phenylmagnesium bromide	3 hr.	97%
E	1,4-Dimethyl-2-chlorobenzene	Phenylmagnesium bromide	3 hr.	85%
F	1,3-Dimethyl-2-chlorobenzene	Phenylmagnesium bromide	5 hr.	87%
G	Methyl-4-bromo-benzoate	Phenylmagnesium bromide	5 hr.	69%
H	4-Iodophenol	Phenylmagnesium bromide	3 hr.	96%
I	4-Chlorophenol	Phenylmagnesium bromide	5 hr.	95%
J	6-Methoxy-2-bromonaphthalene	Phenylmagnesium bromide	1 hr.	98%
K	1-Methoxy-4-chlorobenzene	4-Methylphenylmagnesium bromide	3 hr.	99%



L	1-Methoxy-4-chlorobenzene	3-Methylphenylmagnesium bromide	3 hr.	83%
M	1-Methoxy-4-chlorobenzene	2-Fluorophenylmagnesium bromide	3 hr.	99%
N	1-Methoxy-4-chlorobenzene	2,4,6-Trimethylphenylmagnesium bromide	3 hr.	95%
O	1,3-Dimethyl-2-chlorobenzene	2,4,6-Trimethylphenylmagnesium bromide	24 hr.	0
P	1,3,5-Trimethyl-2-bromobenzene	2,4,6-Trimethylphenylmagnesium bromide	24 hr.	0

### EXAMPLE 15

Reagents, analyses, and procedures were as described in Example 13, except as follows. In all runs, the  $\text{Pd}_2(\text{dibenzylideneacetone})_3$  was used in the amount of 0.02 mmol; the solvent was 1,4-dioxane; the 1,3-bis(substituted)imidazolinium chloride used was 1,3-bis(2,6-diisopropylphenyl)imidazolinium chloride in the amount of 0.02 mmol. All runs were performed at 80°C for 48 hours. Several different aryl chlorides (1.0 mmol each) and Grignard reagents (1.2 mmol each) were used.

The aryl chlorides and Grignard reagents used in each run are listed in Table 14. All of the yields reported in Table 14 are of the heterocoupling product, and are the average of two runs.

TABLE 14

Run	Aryl halide	Grignard reagent	Isolated yield
a	4-Chorotoluene	Vinylmagnesium bromide	26%
b	1-Methoxy-4-chlorobenzene	Vinylmagnesium bromide	14%
c	Methyl-4-chloro-benzoate	Vinylmagnesium bromide	10%
d	4-Chorotoluene	<i>n</i> -Butylmagnesium bromide	8%
e	4-Chorotoluene	<i>sec</i> -Butylmagnesium bromide	16%

### EXAMPLE 16

Reagents, analyses, and procedures were as described in Example 13, except as follows. In all runs, the  $\text{Pd}_2(\text{dibenzylideneacetone})_3$  was used in the amount of 0.02 mmol; the

solvent was 1,4-dioxane; the 1,3-bis(substituted)imidazolinium chloride used was 1,3-bis(2,6-diisopropylphenyl)imidazolinium chloride in the amount of 0.02 mmol. All runs were performed at 80°C for 48 hours. Several different aryl tosylates (1.0 mmol each) and an aryl triflate (1.0 mmol) were used. Homocoupling products of the aryl triflates and the aryl tosylates were observed in all runs other than Run A.

The aryl pseudohalides used in each run are listed in Table 15. All reactions yielded the homocoupling product of the aryl pseudohalide.

TABLE 15

Run	Aryl pseudohalide	Principal product
A	4-Methylphenyl triflate	Homocoupling product of aryl triflate
B	4-Methylphenyl triflate	Homocoupling product of aryl triflate
C	4-Methoxyphenyl triflate	Homocoupling product of aryl triflate
D	4-CH <sub>3</sub> CO <sub>2</sub> -phenyl triflate	Homocoupling product of aryl triflate
E	4-Methylphenyl tosylate	Homocoupling product of aryl tosylate

Example 16 demonstrates that the process of this invention is useful in the homocoupling of aryl triflates and aryl tosylates.

#### Organotin Compound as Transmetalating Agent

The liquid medium for the processes of this invention can include any of a wide range of solvents, and mixtures of solvents are also usable. The exclusion of water is not necessary, but is preferred. Types of solvents that can be used include hydrocarbons, ethers, amides, ketones, and alcohols. Polar solvents are preferred; ethers are a more preferred solvent type. Ethers that may be used include, for example, diethyl ether, di-*n*-propyl ether, diisopropyl ether, *tert*-butyl ethyl ether, diheptyl ether, 1,3-dioxolane, 1,4-dioxane, tetrahydrofuran, methyl tetrahydrofuran, glyme (the dimethyl ether of ethylene glycol), diglyme (the dimethyl ether of diethylene glycol), and the like. Cyclic ethers and polyethers are preferred; a highly preferred ether is 1,4-dioxane.

A large variety of strong bases are suitable for use in the processes of this invention. Generally, these are inorganic bases. Alkali metal salts are a preferred group of inorganic

bases. Examples of suitable alkali metal salts include, but are not limited to, lithium carbonate, lithium *tert*-butoxide, sodium acetate, sodium bicarbonate, sodium *tert*-butoxide, sodium oxide, sodium tetrafluoroborate, potassium acetate, potassium carbonate, potassium *tert*-butoxide, potassium nitrite, potassium phosphate, potassium sulfite, potassium hexafluorophosphate, cesium acetate, cesium bicarbonate, cesium carbonate, cesium fluoride, cesium nitrate, and cesium sulfate. Alkali metal salts of carboxylic acid anions (*e.g.*, acetate, trifluoroacetate, citrate, formate, oxalate, propionate, tartrate, etc.) are also suitable for use as the inorganic base in this invention. More preferred are salts of potassium and cesium; most preferred are cesium salts. The most highly preferred inorganic base is cesium fluoride. Choice(s) of inorganic base will vary with the particular system of aryl halide or pseudohalide and organotin compound involved. Amine bases are generally not preferred because, to date, they appear to poison the catalyst system of the invention.

Directly bonded to the aromatic ring(s) of the aryl halide or pseudohalide (*i.e.*, aryl halide or aryl pseudohalide) is at least one halogen atom selected from a chlorine atom, a bromine atom, and an iodine atom, or at least one pseudohalide group. The term "pseudohalide group" includes such groups as *p*-toluenesulfonate (tosylate), and trifluoromethanesulfonate (triflate), methanesulfonate (meslyate), nonaflate ( $\text{ON}_f$ ), and aryl diazonium salts ( $\text{ArN}_2^+\text{X}^-$ , where  $\text{X}^-$  is halide,  $\text{BF}_4^-$ , etc.). The aryl halide or pseudohalide can have two or more such halogen atoms with an atomic number greater than nine and/or pseudohalide groups, including combinations of halogen atoms and pseudohalide groups. However, when two or more such groups are present, the halogen atoms with an atomic number greater than nine and/or pseudohalide groups should all be different from each other. For example, when two such substituents are present, they may be a chlorine atom and a bromine atom, or an iodine atom and a tosylate group, or *etc.* It is preferred that there is only one chlorine atom, bromine atom, iodine atom, or pseudohalide group directly bound to the aryl ring of the aryl halide or pseudohalide. Aryl chlorides are more preferred as the aryl halide reactants. To prevent self-reaction, it is preferred that stannyl groups are not present on the aryl halide or pseudohalide.

The aryl moiety for the aryl halide or pseudohalide can be homocyclic or heterocyclic. Examples of suitable homocyclic aryl moieties include, but are not limited to, benzene, naphthalene, anthracene, phenanthrene, pyrene, biphenyl, acenaphthalene, fluorene, and

indene. Heterocyclic aryl moieties that can be used include, for example, furan, thiophene, oxathiolane, thianthrene, isobenzofuran, phenoxathiin, and the like. Nitrogen-containing heterocycles that can be used include, for example, pyridine, indole, and isoxazole, and the like. Benzene is a preferred aryl moiety for the aryl halide or pseudohalide.

For the aryl halide or pseudohalide, substituents other than a chlorine atom, a bromine atom, an iodine atom, and/or a pseudohalide group that may be present on the aromatic ring(s) include, but are not limited to, hydrogen atoms, fluorine atoms, nitro groups, hydrocarbyl groups, alkoxy groups, perfluorohydrocarbyl groups, silyl groups, ether groups, ketone groups, and ester groups. When hydrocarbyl groups are present, they are preferably  $C_1$  to  $C_{18}$  alkyl groups or  $C_6$  to  $C_{20}$  aryl or aralkyl groups. Examples of suitable hydrocarbyl groups are methyl, ethyl, isopropyl, *tert*-butyl, cyclopentyl, methylcyclohexyl, decyl, phenyl, tolyl, xylyl, benzyl, naphthyl, and tetrahydronaphthyl. Alkoxy group substituents preferably have  $C_1$  to  $C_6$  alkyl moieties. Some examples of alkoxy groups are methoxy, ethoxy, isopropoxy, methylcyclopentoxy, and cyclohexoxy. Perfluorohydrocarbyl groups include alkyl and aryl perfluorocarbons; suitable perfluorohydrocarbyl groups are, for example, trifluoromethyl, pentafluoroethyl, pentafluorophenyl, and heptafluoronaphthyl. Substituent silyl groups preferably have  $C_1$  to  $C_{18}$  alkyl groups or  $C_6$  to  $C_{20}$  aryl or aralkyl groups, and examples include trimethylsilyl, triisopropylsilyl, *tert*-butyl(dimethyl)silyl, tridecylsilyl, and triphenylsilyl. The substituents preferred for the aryl halide or pseudohalide will depend on the product that is desired.

When an aryl moiety is the unsaturated group of the organotin compound, the aryl moiety can be homocyclic or heterocyclic, as described for the aryl halide or pseudohalide. For the organotin compound, the preferred aryl moieties are benzene and naphthalene. Substituents on the aryl ring, again as described for the aryl halide or pseudohalide, can be hydrogen atoms, fluorine atoms, nitro groups, hydrocarbyl groups, alkoxy groups, perfluorohydrocarbyl groups, silyl groups, ether groups, ketone groups, and ester groups. To prevent self-reaction, it is preferred that chlorine atoms, bromine atoms, iodine atoms, and/or pseudohalide groups are not present on aromatic ring(s) in the organotin compound. In other words, the aryl moiety of the organotin compound is preferably devoid of halogen atoms with an atomic number greater than nine, and preferably is also devoid of pseudohalide groups. However, one or more fluorine atoms can be present on the aromatic ring(s). Preferred

unsaturated groups for the organotin compound depend on the desired product.

The unsaturated group of the organotin compound, when not an aryl moiety, may be a vinyl, allyl, alkenyl, or benzyl moiety. Suitable unsaturated groups are vinyl, allyl, benzyl, butenyl, cyclobutenyl, 2-pentenyl, cyclohexenyl, hexenyl, 1-heptenyl, 2-octenyl, and the like. A large variety of substituents, as described for the aryl moieties, can be present in the unsaturated group.

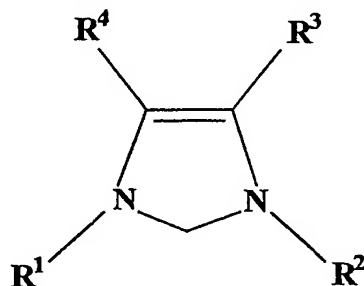
The saturated groups of the organotin compound may be the same or different, and are preferably saturated hydrocarbyl groups. These hydrocarbyl groups can be branched, straight chain, or cyclic. More preferred are hydrocarbyl groups containing from one to ten carbon atoms. Examples of suitable groups include, but are not limited to, methyl, ethyl, isopropyl, *n*-butyl, *sec*-butyl, 2-pentyl, cyclopentyl, methylcyclohexyl, heptyl, octyl, nonyl, and decyl. Especially preferred saturated groups for the organotin compound are methyl groups and *n*-butyl groups; it is also preferred that all of the saturated groups are the same.

Organotin compounds suitable for use in this invention include, but are not limited to, phenyl(trimethyl)tin, trimethyl(3-methylbenzyl)tin, triethyl(pentafluorophenyl)tin, triethyl(vinyl)tin, (allyl)tripropyltin, tripropyl(*o*-tolyl)tin, *trin*-butyl(vinyl)tin, *trin*-butyl(1-ethoxyvinyl)tin, and *trin*-butyl(3-methyl-2-butenyl)tin.

The metal compound comprises at least one metal atom selected from nickel, palladium, and platinum having a formal oxidation state of zero or two, and is sometimes referred to hereinafter as the metal compound. Inorganic salts of nickel, palladium, or platinum that can be used include the bromides, chlorides, fluorides, iodides, cyanides, nitrates, sulfides, sulfites, and sulfates. Organic nickel, palladium, or platinum compounds that may be used include complexes and salts such as the carboxylates, *e.g.*, the acetates or propionates, *etc.* Suitable nickel compounds include bis(1,5-cyclooctadiene)nickel, nickel acetate, nickel oxalate, nickel phosphate, nickel stearate, nickel acetylacetonate, nickel tetrafluoroborate, nickel thiocyanate, nickel carbonate, and nickel sulfamate. Examples of palladium compounds include Pd(OAc)<sub>2</sub>, palladium(II) chloride, Pd(CH<sub>3</sub>CN)<sub>4</sub>(BF<sub>4</sub>)<sub>2</sub>, PdCl<sub>2</sub>(CH<sub>3</sub>CN)<sub>2</sub>, PdCl<sub>2</sub>(PhCN)<sub>2</sub>, PdCl<sub>2</sub>(PPh<sub>3</sub>)<sub>2</sub>, tris(dibenzylideneacetone)dipalladium(0) [which is also referred to herein as dipalladium tris(dibenzylideneacetone)], and palladium trifluoroacetate. Platinum compounds that can be used include platinum acetylacetonate and platinum chloride. Nickel and palladium compounds are preferred; more preferred are

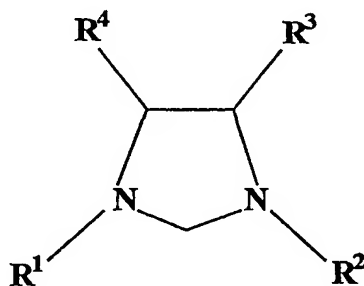
compounds of palladium. Palladium compounds such as palladium acetate and tris(dibenzylideneacetone)dipalladium(0) are most preferred.

Preferred types of N-heterocyclic carbenes are imidazoline-2-ylidenes of the formula



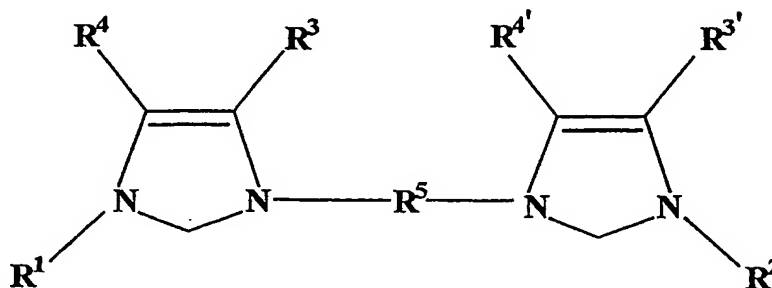
or protonated salts thereof, wherein R¹ and R² are each, independently, alkyl or aryl groups having at least 3 carbon atoms, R³ and R⁴ are each, independently, a hydrogen atom, a halogen atom, or a hydrocarbyl group;

imidazolidine-2-ylidenes of the formula



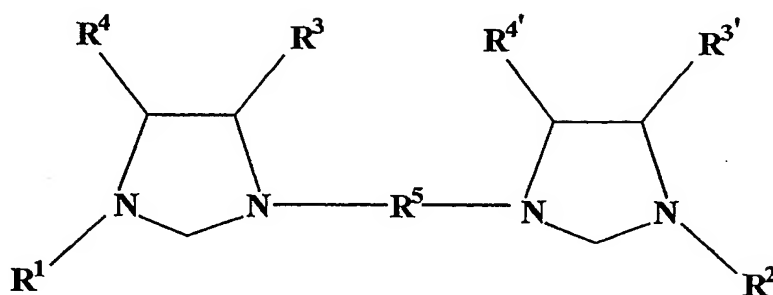
or protonated salts thereof, wherein R¹, R², R³, and R⁴ are as defined for the imidazoline-2-ylidenes;

bis(imidazoline-2-ylidene)s of the formula



or protonated salts thereof, wherein  $R^1$ ,  $R^2$ ,  $R^3$ , and  $R^4$  are as defined for the imidazoline-2-ylidenes, wherein  $R^{3'}$  and  $R^{4'}$  are as defined for  $R^3$  and  $R^4$  for the imidazoline-2-ylidenes, and wherein  $R^5$  is a bridging group that links the two imidazoline rings;

bis(imidazolidine-2-ylidene)s of the formula



or protonated salts thereof, wherein  $R^1$ ,  $R^2$ ,  $R^3$ , and  $R^4$  are as defined for the imidazoline-2-ylidenes, wherein  $R^{3'}$  and  $R^{4'}$  are as defined for  $R^3$  and  $R^4$  for the imidazoline-2-ylidenes, and wherein  $R^5$  is a bridging group that links the two imidazolidine rings.

$R^1$  and  $R^2$  are preferably sterically bulky groups. Suitable groups include, but are not limited to, isopropyl, *sec*-butyl, *tert*-butyl, 2,2-dimethylpropyl (neopentyl), cyclohexyl, norbornyl, adamantyl, tolyl, 3,5-dimethylphenyl, 2,4,6-trimethylphenyl, 2,6-diisopropylphenyl, 2,4,6-triisopropylphenyl, and triphenylmethyl. Preferred groups are *tert*-butyl, 2,4,6-trimethylphenyl, 2,6-diisopropylphenyl, and triphenylmethyl. Most preferred for both  $R^1$  and  $R^2$  are the 2,4,6-trimethylphenyl, 2,6-diisopropylphenyl, and 2,4,6-triisopropylphenyl groups.

Examples of suitable  $R^3$ ,  $R^4$ ,  $R^{3'}$ , and  $R^{4'}$  groups include chlorine atoms, bromine atoms, hydrogen atoms, hydrocarbyl groups, and the like. When hydrocarbyl groups are present, they are preferably  $C_1$  to  $C_{18}$  alkyl groups or  $C_6$  to  $C_{20}$  aryl or aralkyl groups. Examples of suitable hydrocarbyl groups are methyl, ethyl, isopropyl, *tert*-butyl, cyclopentyl, methylcyclohexyl, decyl, phenyl, tolyl, xylyl, benzyl, naphthyl, and tetrahydronaphthyl.

Chlorine atoms and hydrogen atoms are preferred groups. Most preferred for all substituents  $R^3$ ,  $R^4$ ,  $R^{3'}$ , and  $R^{4'}$  are hydrogen atoms.

$R^5$  in both the formula for the bis(imidazoline-2-ylidene)s and the bis(imidazolidine-2-ylidene)s of this invention can be selected from a large variety of moieties, including alkylene groups, arylene groups, and silylene groups. Atoms that can form the bridge include, but are not limited to, carbon, nitrogen, oxygen, silicon, and sulfur. Examples of suitable bridging moieties include methylene ( $-\text{CH}_2-$ ), substituted methylene, ethylene ( $-\text{CH}_2\text{CH}_2-$ ), substituted ethylene, silylene ( $>\text{SiR}_2$ ), benzo ( $\text{C}_6\text{H}_4<$ ), substituted benzo, biphenylene, substituted biphenylene, binaphthylene, and substituted binaphthylene. Heterocyclic aromatic moieties such as, for example, pyridine, pyrimidine, pyrazine, pyridazine, furan, thiophene, oxathiolane, thianthrene, isobenzofuran, phenoxathiin, isothiazole, phenoxazine, and the like, can also form the bridge. Preferred  $R^5$  moieties include biphenylene, binaphthylene, and substituted benzo, with substituted benzo being more preferred. Highly preferred is benzo substituted with methyl groups. The bridge has at least one atom, and preferably has from four to eight atoms. While better results have been observed with longer bridges, it is possible that judicious choices for  $R^1$ ,  $R^2$ ,  $R^3$ ,  $R^4$ ,  $R^{3'}$ , and  $R^{4'}$  may improve results for short bridges.

Without being bound by theory, it appears from thermochemical studies that the electron-donating ability of many of the imidazoline-2-ylidene carbene ligands is better than that of tri(cyclohexyl)phosphine and the steric demand of these carbene ligands is greater than that of tri(cyclohexyl)phosphine. This suggests that the N-heterocyclic carbene should possess steric bulk sufficient to stabilize both the free carbene and to stabilize reaction intermediates. However, imidazoline-2-ylidene carbenes and imidazolidine-2-ylidene carbenes are considerably less stable to air and moisture than their corresponding protonated imidazolium and imidazolidinium salts. Thus, a highly preferred embodiment of this invention involves generation of the imidazoline-2-ylidene *in situ* from the corresponding imidazolium salt (similarly so for the imidazolidine-2-ylidene and the corresponding imidazolidinium salt); this removes the need to handle the N-heterocyclic carbene ligands in an inert atmosphere. Protonated salts of the imidazoline-2-ylidene carbenes and imidazolidine-2-ylidene carbenes are monoprotonated, while the protonated salts of the bis(imidazoline-2-ylidene)s and the bis(imidazolidine-2-ylidene)s are diprotonated. Suitable counterions for the protonated salts are virtually limitless, but halides are preferred



counterions. The most preferred counterions are chloride and bromide. The imidazolinium salts are straightforward to synthesize and are air-stable. While the absence of oxygen is not necessary when using a protonated salt of an imidazoline-2-ylidene carbene or an imidazolidine-2-ylidene carbene, it is preferred. When using a neutral carbene, the absence of oxygen is necessary. In any instance where oxygen is excluded, the presence of an inert gas such as nitrogen, helium, or argon is preferred.

The aryl halide or pseudohalide and the organotin compound may be employed in an ideal molar ratio of about 1:1 when using an aryl halide or pseudohalide that has only one halogen atom (other than a fluorine atom) or pseudohalide group; or either reagent may be used in excess. It is preferred to use the organotin compound in an excess such that the molar ratio of aryl halide or pseudohalide to organotin compound is in the range of from about 1:1 to about 1:3 when using an aryl halide or pseudohalide that has only one halogen atom (other than a fluorine atom) or pseudohalide group. When the aryl halide or pseudohalide has more than one halogen atom (other than fluorine) and/or pseudohalide group, reactions may be carried out in sequence. An organotin compound will react first at the site of the more reactive substituent, *e.g.*, at iodine before bromine. Reaction at only the site of the more reactive substituent(s) can be performed. In reactions carried out in sequence where the organotin compounds are different, each should be added separately. It is preferred to allow one reaction to finish before the addition of the next organotin compound. When different organotin compounds are used, it is preferred to use close to the ideal molar ratio of aryl halide or pseudohalide to organotin compound to minimize undesirable side products.

A suitable molar ratio of aryl halide or pseudohalide to strong base is in the range of from about 1:1 to about 1:5. A more preferred molar ratio of aryl halide or pseudohalide to strong base is in the range of from about 1:1 to about 1:3.

Normally, the molar ratio of metal atoms of the metal compound to aryl halide or pseudohalide molecules is in the range of from about 0.01:1 to about 0.10:1; a preferred molar ratio of metal atoms of metal compound to aryl halide or pseudohalide molecules is in the range of from about 0.03:1 to about 0.07:1. For the metal compound and the carbene ligands, the molar ratio of metal atoms of the metal compound to carbene molecules is in the range of from about 1:0.5 to about 1:5, and more preferably in the range of from about 1:1 to about 1:3.

The order of addition of the various components to a reaction vessel is not of particular importance. Premixing of the components of the catalyst system is not necessary; however, it is preferred that the catalyst system is premixed. To premix the components of the catalyst system, the metal compound, the N-heterocyclic carbene (salt or neutral compound), and the strong base are mixed together after being added in no particular order to a reaction vessel. The mixing time (activation period) for these components on the laboratory scale may be very short, *e.g.*, five minutes or less, but a preferred mixing time is in the range of from about fifteen minutes to about sixty minutes.

If a premixed catalyst system is used, the aryl halide or pseudohalide and the organotin compound may be added to the same reaction vessel, or the premixed catalyst system can be transferred to a different vessel in which the reaction is to take place. Use of the same vessel for premixing the catalyst system and conducting the reaction is preferred.

When the components of the catalyst system are not premixed, the strong base, aryl halide or pseudohalide, the organotin compound, the metal compound, the liquid medium, and the N-heterocyclic carbene (salt or neutral compound) are added in any order to the reaction vessel.

Optionally, one or more salt additives may be included in the reaction mixture. A salt additive may speed the reaction and/or increase the yield of the reaction. Suitable compounds for use as a salt additive include alkali metal halides and alkaline earth halides. Alkali metal halides are preferred; examples of alkali metal halides include lithium chloride, lithium bromide, lithium iodide, sodium chloride, sodium bromide, sodium iodide, potassium chloride, potassium bromide, potassium iodide, cesium chloride, cesium bromide, and cesium iodide. Lithium salts and sodium salts are preferred, especially lithium chloride and sodium iodide.

Once all of the components are present in the same reaction vessel, the mixture may be heated, provided that the temperature does not exceed the thermal decomposition temperature of the catalyst system or the products of the reaction. Preferred temperatures are in the range of from about 20°C to about 150°C; more preferred temperatures are in the range of from about 20°C to about 120°C. When the aryl halide or pseudohalide is an aryl chloride, an aryl triflate, or an aryl tosylate, heat is usually necessary to drive the reaction. Preferred temperatures when the aryl halide or pseudohalide is an aryl chloride, an aryl triflate, or an

aryl tosylate are in the range of from about 40°C to about 150°C. When the aryl halide or pseudohalide is an aryl bromide or an aryl iodide, the reaction(s) proceeds easily at room temperature, although heat may speed the reaction. For aryl bromides and aryl iodides, preferred temperatures are in the range of from about 20°C to about 70°C.

While not necessary when using protonated salts of N-heterocyclic carbenes, the absence of oxygen and water is preferred when conducting the processes of this invention. Conversely, the exclusion of oxygen and water is generally necessary when neutral carbenes are used. The presence of an inert gas such as argon or nitrogen is preferred when oxygen and/or water are excluded. The reaction mixture is normally agitated. A preferred contact time for the components of the reaction is in the range of from about one hour to about seventy-two hours. More preferably, the contact time is from about one hour to about forty-eight hours.

The following examples are presented for purposes of illustration, and are not intended to impose limitations on the scope of this embodiment of the invention.

## EXAMPLES 17-18

### GENERAL PROCEDURES

**Reagents.** The synthesis of 1,3-bis(2,6-diisopropylphenyl)imidazolinium chloride was carried out in a fashion similar to that reported in U.S. Patent No. 5,077,414, and/or Arduengo, A. J. III., Dias, H.V.R.; Harlow, R.L. and Kline, M. *J. Am. Chem. Soc.*, 1992, **114**, 5530-5534, except that it was done in two steps (rather than in one pot).

**Analyses.** All reactions were monitored by thin layer chromatography (TLC). <sup>1</sup>H and <sup>13</sup>C nuclear magnetic resonance (NMR) spectra were recorded on a 300 MHz NMR spectrometer (Varian, Incorporated) or 400 MHz NMR spectrometer (Varian) at ambient temperature in CDCl<sub>3</sub> (Cambridge Isotope Laboratories, Incorporated).

**Conditions.** All reactions were carried out under an atmosphere of argon in oven-dried glassware with magnetic stirring, unless otherwise indicated.

### EXAMPLE 17

For each run, a Schlenk tube was charged with Pd<sub>2</sub>(dibenzylideneacetone)<sub>3</sub> (28 mg, 0.03 mmol), 1,3-bis(2,6-diisopropylphenyl)imidazolinium chloride (25.5 mg, 0.06 mmol), CsF (334 mg, 2.2 mmol), and a magnetic stirring bar. After a 30 minute catalyst activation

period, 1,4-dioxane (3 mL), an aryl chloride (1.0 mmol each) or an aryl triflate (1 mmol), and  $(C_6H_5)_3Sn(CH_3)_3$  (1.05 mmol) were added in turn to the Schlenk tube. The Schlenk tube was placed in a 100°C oil bath and stirred for 48 hours. The mixture was then allowed to cool to room temperature. The mixture was washed with diethyl ether. The organic layer and the diethyl ether extracts were combined, washed with saturated saline solution, and then dried over  $MgSO_4$ . The solvent was removed under vacuum and the residue was purified by flash chromatography using hexane or a mixture of hexane and ethyl acetate.

The aryl chlorides or aryl triflates used in each run are listed in Table 16. All of the yields reported in Table 16 are of the heterocoupling product, and are the average of two runs.

TABLE 16

Run	Aryl chloride or aryl triflate	Isolated yield
a	4-Chlorotoluene	84%
b	Methyl-4-chlorobenzoate	52%
c	4- $CH_3CO_2$ -phenyl triflate	14%

## EXAMPLE 18

Reagents, analyses, and procedures were as described in Example 17, except as follows. The aryl chloride used in both runs was methyl-4-chlorobenzoate (1.0 mmol); different organotin compounds (1.05 mmol each) were used. The organotin compound used in each run are listed in Table 17. All of the yields reported in Table 17 are of the heterocoupling product, and are the average of two runs.

TABLE 17

Run	Organotin compound	Isolated yield
a	$(CH_2CH)Sn(n-Bu)_3$	63%
b	$(CH_2CHCH_2)Sn(n-Bu)_3$	80%

Silane as Transmetalating Agent

The liquid medium for the processes of this invention can include any of a wide range of solvents, and mixtures of solvents are also usable. The exclusion of water is not necessary, but is preferred. Types of solvents that can be used include hydrocarbons, ethers, amides,

ketones, and alcohols. Polar solvents are preferred; ethers are a more preferred solvent type. Ethers that may be used include, for example, diethyl ether, di-*n*-propyl ether, diisopropyl ether, *tert*-butyl ethyl ether, diheptyl ether, 1,3-dioxolane, 1,4-dioxane, tetrahydrofuran, methyltetrahydrofuran, glyme (the dimethyl ether of ethylene glycol), diglyme (the dimethyl ether of diethylene glycol), and the like. Cyclic ethers and polyethers are preferred; a highly preferred ether is 1,4-dioxane.

A variety of strong bases can be used in the processes of this invention. Fluoride salts are a preferred group of bases. Preferable counterions for the fluoride anion are alkali metal cations and ammonium cations. When an alkali metal fluoride is used, it can be lithium fluoride, sodium fluoride, potassium fluoride, rubidium fluoride, or cesium fluoride, and is preferably cesium fluoride. It is more preferable to use an ammonium fluoride. Suitable substituents for the ammonium cation include hydrogen atoms and hydrocarbyl groups, whether straight chain, branched, or cyclic. Preferred hydrocarbyl substituents have from 1 to about 10 carbon atoms. Examples of ammonium fluoride salts that can be used in this invention include, but are not limited to, ammonium fluoride (NH<sub>4</sub>F), trimethylammonium fluoride, tetramethylammonium fluoride, phenyltrimethylammonium fluoride, benzyltrimethylammonium fluoride, tetraethylammonium fluoride, tetrapropylammonium fluoride, diisopropylammonium fluoride, isopropylcyclohexylammonium fluoride, tetrabutylammonium fluoride, diisobutylammonium fluoride, cyclopentylammonium fluoride, dicyclohexylammonium fluoride, heptylammonium fluoride, tetraoctylammonium fluoride, dinonylammonium fluoride, *n*-decylammonium fluoride, and tribenzylammonium fluoride. It is preferred that all four substituents of the ammonium cation are hydrocarbyl groups. Preferred ammonium fluoride salts are tetramethylammonium fluoride, tetrabutylammonium fluoride, and tetraoctylammonium fluoride, especially tetrabutylammonium fluoride. Choice(s) of base will vary with the particular system of aryl halide or pseudohalide and silane involved.

Directly bonded to the aromatic ring(s) of the aryl halide or pseudohalide (*i.e.*, aryl halide or aryl pseudohalide) is at least one halogen atom selected from a chlorine atom, a bromine atom, and an iodine atom, or at least one pseudohalide group. The term "pseudohalide group" includes such groups as *p*-toluenesulfonate (tosylate), trifluoromethanesulfonate (triflate), methanesulfonate (mesylate), nonaflate (ON<sub>9</sub>), and aryl

diazonium salts ( $\text{ArN}_2^{\oplus}\text{X}^{\ominus}$ , where  $\text{X}^{\ominus}$  is halide,  $\text{BF}_4^{\ominus}$ , *etc.*). The aryl halide or pseudohalide can have two or more such halogen atoms with an atomic number greater than nine and/or pseudohalide groups, including combinations of halogen atoms and pseudohalide groups. However, when two or more such groups are present, the halogen atoms with an atomic number greater than nine and/or pseudohalide groups should all be different from each other. For example, when two such substituents are present, they may be a chlorine atom and a bromine atom, or an iodine atom and a tosylate group, or *etc.* It is preferred that there is only one chlorine atom, bromine atom, iodine atom, or pseudohalide group directly bound to the aryl ring of the aryl halide or pseudohalide. Aryl chlorides are more preferred as the aryl halide reactants. To prevent self-reaction, it is preferred that silyl groups are not present on the aryl halide or pseudohalide.

The aryl moiety for the aryl halide or pseudohalide can be homocyclic or heterocyclic. Examples of suitable homocyclic aryl moieties include, but are not limited to, benzene, naphthalene, anthracene, phenanthrene, pyrene, biphenyl, acenaphthalene, fluorene, and indene. Heterocyclic aryl moieties that can be used include, for example, furan, thiophene, pyridine, indole, oxathiolane, isoxazole, thianthrene, isobenzofuran, phenoxathiin, and the like. Benzene is a preferred aryl moiety for the aryl halide or pseudohalide.

For the aryl halide or pseudohalide, substituents other than a chlorine atom, a bromine atom, an iodine atom, and/or a pseudohalide group that may be present on the aromatic ring(s) include, but are not limited to, hydrogen atoms, fluorine atoms, nitro groups, hydrocarbyl groups, alkoxy groups, perfluorohydrocarbyl groups, ether groups, ketone groups, and ester groups. When hydrocarbyl groups are present, they are preferably  $\text{C}_1$  to  $\text{C}_{18}$  alkyl groups or  $\text{C}_6$  to  $\text{C}_{20}$  aryl or aralkyl groups. Examples of suitable hydrocarbyl groups are methyl, ethyl, isopropyl, *tert*-butyl, cyclopentyl, methylcyclohexyl, decyl, phenyl, tolyl, xylyl, benzyl, naphthyl, and tetrahydronaphthyl. Alkoxy group substituents preferably have  $\text{C}_1$  to  $\text{C}_6$  alkyl moieties. Some examples of alkoxy groups are methoxy, ethoxy, isopropoxy, methylcyclopentoxy, and cyclohexoxy. Perfluorohydrocarbyl groups include alkyl and aryl perfluorocarbons; suitable perfluorohydrocarbyl groups are, for example, trifluoromethyl, pentafluoroethyl, pentafluorophenyl, and heptafluoronaphthyl. The substituents preferred for the aryl halide or pseudohalide will depend on the product that is desired.

When an aryl moiety is the unsaturated group of the silane, the aryl moiety can be

homocyclic or heterocyclic, as described for the aryl halide or pseudohalide. For the silane, the preferred aryl moieties are benzene and naphthalene. Substituents on the aryl ring, again as described for the aryl halide or pseudohalide, can be hydrogen atoms, fluorine atoms, nitro groups, hydrocarbyl groups, alkoxy groups, perfluorohydrocarbyl groups, ether groups, ketone groups, and ester groups. To prevent self-reaction, it is preferred that chlorine atoms, bromine atoms, iodine atoms, and/or pseudohalide groups are not present on aromatic ring(s) in the silane. In other words, the aryl moiety of the silane is preferably devoid of halogen atoms with an atomic number greater than nine, and preferably is also devoid of pseudohalide groups. However, one or more fluorine atoms can be present on the aromatic ring(s). Preferred unsaturated groups for the silane depend on the desired product.

The unsaturated group of the silane, when not an aryl moiety, may be a vinyl, allyl, alkenyl, benzyl, or aryloxy moiety. Suitable unsaturated groups are vinyl, allyl, benzyl, 1-butenyl, 1-cyclobutenyl, 2-pentenyl, cyclohexenyl, 1-hexenyl, 1-heptenyl, 2-octenyl, phenoxy, naphthoxy, biphenyloxy, phenanthroxy, fluorenoxy, and the like. A large variety of substituents, as described for the aryl moieties, can be present in the unsaturated group.

The saturated groups of the silane may be the same or different, and are preferably saturated hydrocarbyl or saturated hydrocarbyloxy groups. The saturated hydrocarbyl groups can be branched, straight chain, or cyclic. More preferred are hydrocarbyl groups containing from one to ten carbon atoms. Examples of suitable groups include, but are not limited to, methyl, ethyl, isopropyl, *n*-butyl, *sec*-butyl, 2-pentyl, cyclopentyl, methylcyclohexyl, heptyl, octyl, nonyl, and decyl. Much as described for the saturated hydrocarbyl groups, the hydrocarbyl portion of the saturated hydrocarbyloxy groups can be branched, straight chain, or cyclic. Similarly, hydrocarbyl portions of the saturated hydrocarbyloxy groups containing from one to ten carbon atoms are more preferred. Suitable saturated hydrocarbyloxy groups include methoxy, ethoxy, propoxy, isopropoxy, *n*-butoxy, *tert*-butoxy, cyclobutoxy, 3-pentoxo, 4-methylcyclohexoxy, 4-heptoxy, 1-octoxy, 2-nonoxo, and 1-decoxy. Especially preferred saturated groups for the silane are methyl groups and methoxy groups; it is also preferred that all of the saturated groups are the same.

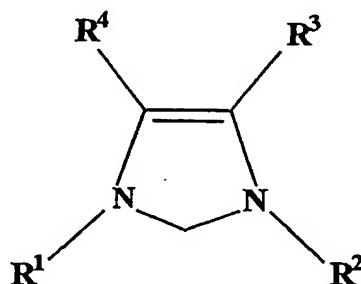
Silanes suitable for use in this invention include, but are not limited to, vinyltrimethylsilane, phenyl(trimethyl)silane, trimethyl(3-methylbenzyl)silane, (6-methoxy-2-naphthyl)trimethylsilane, triethyl(vinyl)silane, triethyl(pentafluorophenyl)silane,

(allyl)tripropylsilane, tripropyl(*o*-tolyl)silane, tri-*n*-butyl(3-methyl-2-butenyl)silane, tri-*n*-butyl(vinyl)silane, vinyltrimethoxysilane, phenyltrimethoxysilane, (6-methoxy-2-naphthyl)trimethoxysilane, naphthyltriisopropoxysilane, phenyldimethoxyisopropoxysilane, phenoxytriisopropylsilane, naphthoxyethyl dimethylsilane, (6-methoxy-2-naphthoxy)trimethoxysilane, and phenanthroxyltrimethoxysilane.

The metal compound comprises at least one metal atom selected from nickel, palladium, and platinum having a formal oxidation state of zero or two, and is sometimes referred to hereinafter as the metal compound. Inorganic salts of nickel, palladium, or platinum that can be used include the bromides, chlorides, fluorides, iodides, cyanides, nitrates, sulfides, sulfites, and sulfates. Organic nickel, palladium, or platinum compounds that may be used include complexes and salts such as the carboxylates, *e.g.*, the acetates or propionates, *etc.* Suitable nickel compounds include bis(1,5-cyclooctadiene)nickel, nickel acetate, nickel oxalate, nickel phosphate, nickel stearate, nickel acetylacetonate, nickel tetrafluoroborate, nickel thiocyanate, nickel carbonate, and nickel sulfamate. Examples of palladium compounds include Pd(OAc)<sub>2</sub>, palladium(II) chloride, Pd(CH<sub>3</sub>CN)<sub>4</sub>(BF<sub>4</sub>)<sub>2</sub>, tris(dibenzylideneacetone)dipalladium(0) [which is also referred to herein as dipalladium tris(dibenzylideneacetone)], and palladium trifluoroacetate. Platinum compounds that can be used include platinum acetylacetonate and platinum chloride. Nickel and palladium compounds are preferred; more preferred are compounds of palladium. Palladium compounds such as palladium acetate and tris(dibenzylideneacetone)dipalladium(0) are most preferred.

Preferred types of N-heterocyclic carbenes are

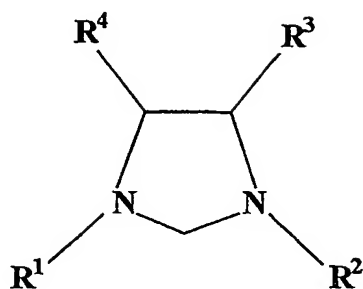
A) imidazoline-2-ylidenes of the formula



or protonated salts thereof, wherein at least R<sup>1</sup> or R<sup>2</sup> is an alkyl or aryl group having at least 3 carbon atoms, R<sup>3</sup> and R<sup>4</sup> are each, independently, a hydrogen atom, a halogen atom, or a hydrocarbyl group;

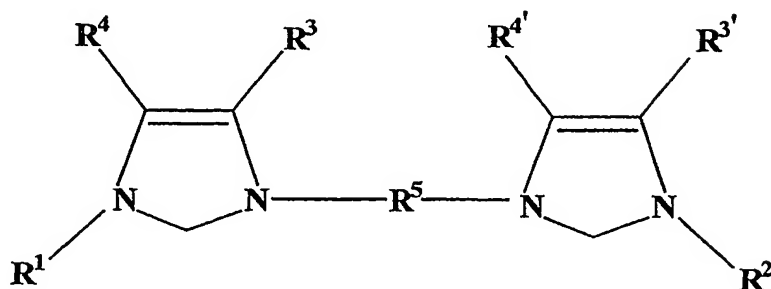


B) imidazolidine-2-ylidenes of the formula



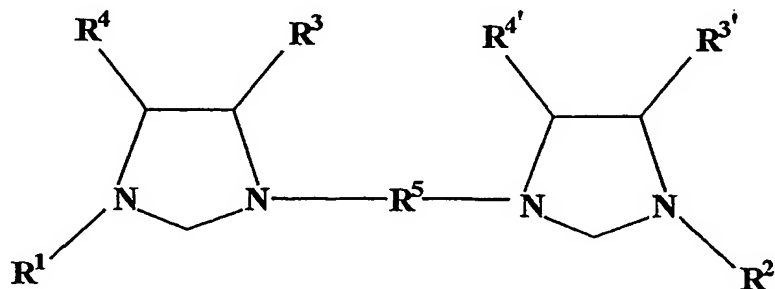
or protonated salts thereof, wherein  $R^1$ ,  $R^2$ ,  $R^3$ , and  $R^4$  are as defined for the imidazolidine-2-ylidenes;

C) bis(imidazolidine-2-ylidene)s of the formula



or protonated salts thereof, wherein  $R^1$ ,  $R^2$ ,  $R^3$ , and  $R^4$  are as defined for the imidazolidine-2-ylidenes, wherein  $R^{3'}$  and  $R^{4'}$  are as defined for  $R^3$  and  $R^4$  for the imidazolidine-2-ylidenes, and wherein  $R^5$  is a bridging group that links the two imidazolidine rings;

D) bis(imidazolidine-2-ylidene)s of the formula



or protonated salts thereof, wherein  $R^1$ ,  $R^2$ ,  $R^3$ , and  $R^4$  are as defined for the imidazoline-2-ylidenes, wherein  $R^{3'}$  and  $R^{4'}$  are as defined for  $R^3$  and  $R^4$  for the imidazoline-2-ylidenes, and wherein  $R^5$  is a bridging group that links the two imidazolidine rings.

It is preferred that both  $R^1$  and  $R^2$  are secondary or tertiary groups. More preferably,  $R^1$  and  $R^2$  are sterically bulky groups. Suitable groups include, but are not limited to, isopropyl, *sec*-butyl, *tert*-butyl, 2,2-dimethylpropyl (neopentyl), cyclohexyl, norbornyl, adamantyl, tolyl, 3,5-dimethylphenyl, 2,4,6-trimethylphenyl, 2,6-diisopropylphenyl, and triphenylmethyl. Preferred groups are *tert*-butyl, 2,4,6-trimethylphenyl, 2,6-diisopropylphenyl, and triphenylmethyl. Most preferred for both  $R^1$  and  $R^2$  are the 2,4,6-trimethylphenyl and 2,6-diisopropylphenyl groups.

Examples of suitable  $R^3$ ,  $R^4$ ,  $R^{3'}$ , and  $R^{4'}$  groups include chlorine atoms, bromine atoms, hydrogen atoms, hydrocarbyl groups, and the like. When hydrocarbyl groups are present, they are preferably  $C_1$  to  $C_{18}$  alkyl groups or  $C_6$  to  $C_{20}$  aryl or aralkyl groups. Examples of suitable hydrocarbyl groups are methyl, ethyl, isopropyl, *tert*-butyl, cyclopentyl, methylcyclohexyl, decyl, phenyl, tolyl, xylyl, benzyl, naphthyl, and tetrahydronaphthyl. Chlorine atoms and hydrogen atoms are preferred groups. Most preferred for all substituents  $R^3$ ,  $R^4$ ,  $R^{3'}$ , and  $R^{4'}$  are hydrogen atoms.

$R^5$  in both the formula for the bis(imidazoline-2-ylidene)s and the bis(imidazolidine-2-ylidene)s of this invention can be selected from a large variety of moieties, including alkylene groups, arylene groups, and silylene groups. Atoms that can form the bridge include, but are not limited to, carbon, nitrogen, oxygen, silicon, and sulfur. Examples of suitable bridging moieties include methylene ( $-CH_2-$ ), substituted methylene, ethylene ( $-CH_2CH_2-$ ), substituted ethylene, silylene ( $>SiR_2$ ), benzo ( $C_6H_4<$ ), substituted benzo, biphenylene, substituted biphenylene, binaphthylene, and substituted binaphthylene. Heterocyclic aromatic moieties such as, for example, pyridine, pyrimidine, pyrazine, pyridazine, furan, thiophene, oxathiolane, thianthrene, isobenzofuran, phenoxathiin, isothiazole, phenoxazine, and the like, can also form the bridge. Preferred  $R^5$  moieties include biphenylene, binaphthylene, and substituted benzo, with substituted benzo being more preferred. Highly preferred is benzo substituted with methyl groups. The bridge preferably has at least four atoms, and more

preferably has from four to eight atoms. While better results have been observed with longer bridges, it is possible that judicious choices for  $R^1$ ,  $R^2$ ,  $R^3$ ,  $R^4$ ,  $R^{3'}$ , and  $R^{4'}$  may improve results for short bridges.

Without being bound by theory, it appears from thermochemical studies that the electron-donating ability of many of the imidazoline-2-ylidene carbene ligands is better than that of tri(cyclohexyl)phosphine and the steric demand of these carbene ligands is greater than that of tri(cyclohexyl)phosphine. This suggests that the N-heterocyclic carbene should possess steric bulk sufficient to stabilize both the free carbene and to stabilize reaction intermediates. However, imidazoline-2-ylidene carbenes and imidazolidine-2-ylidene carbenes are considerably less stable to air and moisture than their corresponding protonated imidazolinium and imidazolidinium salts. Thus, a highly preferred embodiment of this invention involves generation of the imidazoline-2-ylidene *in situ* from the corresponding imidazolinium salt (similarly so for the imidazolidine-2-ylidene and the corresponding imidazolidinium salt); this removes the need to handle the N-heterocyclic carbene ligands in an inert atmosphere. Protonated salts of the imidazoline-2-ylidene carbenes and imidazolidine-2-ylidene carbenes are monoprotonated, while the protonated salts of the bis(imidazoline-2-ylidene)s and the bis(imidazolidine-2-ylidene)s are diprotonated. Suitable counterions for the protonated salts are virtually limitless, but halides are preferred counterions. The most preferred counterions are chloride and bromide. The imidazolinium salts are straightforward to synthesize and are air-stable. While the absence of oxygen is not necessary when using a protonated salt of an imidazoline-2-ylidene carbene or an imidazolidine-2-ylidene carbene, it is preferred. When using a neutral carbene, the absence of oxygen is necessary. In any instance where oxygen is excluded, the presence of an inert gas such as nitrogen, helium, or argon is preferred.

The aryl halide or pseudohalide and the silane may be employed in an ideal molar ratio of about 1:1 when using an aryl halide or pseudohalide that has only one halogen atom (other than a fluorine atom) or pseudohalide group; or either reagent may be used in excess. It is preferred to use the silane in an excess such that the molar ratio of aryl halide or pseudohalide to silane is in the range of from about 1:1.5 to about 1:4 when using an aryl halide or pseudohalide that has only one halogen atom (other than a fluorine atom) or pseudohalide group. When the aryl halide or pseudohalide has more than one halogen atom (other than

fluorine) and/or pseudohalide group, reactions may be carried out in sequence. A silane will react first at the site of the more reactive substituent, *e.g.*, at iodine before bromine. Reaction at only the site of the more reactive substituent(s) can be performed. In reactions carried out in sequence where the silanes are different, each should be added separately. It is preferred to allow one reaction to finish before the addition of the next silane. When different silanes are used, it is preferred to use close to the ideal molar ratio of aryl halide or pseudohalide to silane to minimize undesirable side products.

A suitable molar ratio of aryl halide or pseudohalide to strong base is in the range of from about 1:1 to about 1:5. A more preferred molar ratio of aryl halide or pseudohalide to strong base is in the range of from about 1:1 to about 1:3.

Normally, the molar ratio of metal atoms of the metal compound to aryl halide or pseudohalide molecules is in the range of from about 0.01:1 to about 0.05:1; a preferred molar ratio of metal atoms of metal compound to aryl halide or pseudohalide molecules is in the range of from about 0.02:1 to about 0.04:1. For the metal compound and the carbene ligands, the molar ratio of metal atoms of the metal compound to carbene molecules is in the range of from about 1:0.5 to about 1:5, and more preferably in the range of from about 1:1 to about 1:3.

The order of addition of the various components to a reaction vessel is not of particular importance. Premixing of the components of the catalyst system is not necessary; however, it is preferred that the catalyst system is premixed. To premix the components of the catalyst system, the metal compound, the N-heterocyclic carbene (salt or neutral compound), and the strong base are mixed together after being added in no particular order to a reaction vessel. The mixing time (activation period) for these components on the laboratory scale may be very short, *e.g.*, five minutes or less, but a preferred mixing time is in the range of from about fifteen minutes to about sixty minutes.

If a premixed catalyst system is used, the aryl halide or pseudohalide and the silane may be added to the same reaction vessel, or the premixed catalyst system can be transferred to a different vessel in which the reaction is to take place. Use of the same vessel for premixing the catalyst system and conducting the reaction is preferred.

When the components of the catalyst system are not premixed, the strong base, aryl halide or pseudohalide, the silane, the metal compound, the liquid medium, and the N-

heterocyclic carbene (salt or neutral compound) are added in any order to the reaction vessel.

Once all of the components are present in the same reaction vessel, the mixture may be heated, provided that the temperature does not exceed the thermal decomposition temperature of the catalyst system or the products of the reaction. Preferred temperatures are in the range of from about 20 °C to about 150 °C; more preferred temperatures are in the range of from about 20 °C to about 110 °C. When the aryl halide or pseudohalide is an aryl chloride, an aryl triflate, or an aryl tosylate, heat is usually necessary to drive the reaction. Preferred temperatures when the aryl halide or pseudohalide is an aryl chloride, an aryl triflate, or an aryl tosylate are in the range of from about 40 °C to about 150 °C. When the aryl halide or pseudohalide is an aryl bromide or an aryl iodide, the reaction(s) usually proceeds at room temperature, although heat may speed the reaction. For aryl bromides and aryl iodides, preferred temperatures are in the range of from about 20 °C to about 90 °C.

Occasionally, a small amount of homocoupled product is observed. Use of a lower reaction temperature and a larger amount of silane usually decreases the quantity of homocoupling product obtained, thus increasing the yield of the desired heterocoupled product.

While not necessary when using protonated salts of N-heterocyclic carbenes, the absence of oxygen and water is preferred when conducting the processes of this invention. Conversely, the exclusion of oxygen and water is generally necessary when neutral carbenes are used. The presence of an inert gas such as argon or nitrogen is preferred when oxygen and/or water are excluded. The reaction mixture is normally agitated. A preferred contact time for the components of the reaction is in the range of from about one hour to about forty-eight hours. More preferably, the contact time is from about one hour to about twenty-four hours.

The following examples are presented for purposes of illustration, and are not intended to impose limitations on the scope of this embodiment of the invention.

## EXAMPLES 19-23

### GENERAL PROCEDURES

**Reagents.** All aryl chlorides and bromides (Aldrich Chemical Company), tetrabutylammonium fluoride (1.0M in tetrahydrofuran, Aldrich), 1,4-dioxane (anhydrous,

Aldrich), palladium acetate (Strem Chemical Company), and  $\text{Pd}_2(\text{dibenzylideneacetone})_3$  (Strem) were used as received. Flash chromatography was performed on silica gel 60 (230-400 mesh; Natland International Corporation).

1,3-bis(2,4,6-trimethylphenyl)imidazoline-2-ylidene and 1,3-Bis(2,4,6-trimethylphenyl)imidazolinium chloride were prepared according to reported procedures in U.S. Patent No. 5,077,414, and/or Arduengo, A. J. III., Dias, H.V.R.; Harlow, R.L. and Kline, M. *J. Am. Chem. Soc.*, 1992, 114, 5530-5534. The synthesis of 1,3-bis(2,6-diisopropylphenyl)imidazolinium chloride was carried out in a similar fashion, except that it was done in two steps rather than in one pot (see Example 1).

**Analyses.** All reactions were monitored by gas chromatography (GC).  $^1\text{H}$  and  $^{13}\text{C}$  nuclear magnetic resonance (NMR) spectra were recorded on a 300 MHz NMR spectrometer (Varian, Incorporated) or 400 MHz NMR spectrometer (Varian) at ambient temperature in  $\text{CDCl}_3$  (Cambridge Isotope Laboratories, Incorporated). All of the products, which are known compounds, had  $^1\text{H}$  NMR spectra identical with literature data.

**Conditions.** All reactions were carried out under an atmosphere of argon in oven-dried glassware with magnetic stirring, unless otherwise indicated.

#### EXAMPLE 19

2,6-Diisopropylaniline (100g, 0.56 mol), glyoxal (31.5 mL, 40% in water, 0.28 mol), and absolute ethanol (500 mL) were charged to a round-bottom flask. A few drops of formic acid were added, and the solution immediately changed from colorless to yellow. After a few hours, a yellow precipitate appeared. The reaction mixture was stirred for another two days. The yellow precipitate was collected by filtration and washed with cold methanol. 1,4-Bis(2,6-diisopropylphenyl)diazabutadiene was obtained in the amount of 81.74g, a yield of 77.5%.

Toluene (500 mL) and 1,4-Bis(2,6-diisopropylphenyl)diazabutadiene (25g, 66 mol) were added to a reaction vessel, followed by solid paraformaldehyde (2.0g, 66 mmol). The reaction mixture was heated to  $100^\circ\text{C}$  until most of the paraformaldehyde had dissolved. The mixture was then cooled to  $40^\circ\text{C}$ , and HCl (16.5mL, 4 moles per liter in dioxane, 66 mmol) was added *via* syringe. The reaction mixture turned brown in color, and a white precipitate appeared after a few hours. The reaction mixture was stirred at room temperature for another 36 hours. The precipitate was then collected by filtration and washed with tetrahydrofuran.

The yield of 1,3-bis(2,6-diisopropylphenyl)imidazolinium chloride was 13.1g, or 47%.

Imidazolidine-2-ylidenes can be prepared by hydrogenation of the corresponding imidazolinium salt, for example, with KH in tetrahydrofuran. See in this connection Arduengo et al., *J. Am. Chem. Soc.*, 1995, 117, 11027.

#### EXAMPLE 20

For each run, a screw-capped vial with a septum was charged with palladium acetate (6.7 mg, 0.03 mmol), 1,3-bis(2,6-diisopropylphenyl)imidazolinium chloride (13 mg, 0.03 mmol), (*n*Bu)<sub>4</sub>NF (2 mL of a 1.0M solution in tetrahydrofuran, 2.00 mmol), and a magnetic stirring bar. 1,4-dioxane (3 mL), aryl halide (1.0 mmol), and phenyltrimethoxysilane (2.0 mmol) were added in turn to the vial. The vial was placed in a 80 °C oil bath and the mixture was stirred for a number of hours. The mixture was then allowed to cool to room temperature. The reaction mixture was quenched with water (30 mL), and extracted with diethyl ether (4 x 30 mL). The combined diethyl ether extractions were dried over MgSO<sub>4</sub>, concentrated *in vacuo*, and purified by flash chromatography.

Some homocoupled product was formed when 4-bromotoluene was used in this reaction. When 4-bromotoluene was reacted at 60 °C with 3 mmol of phenyltrimethoxysilane, the amount of homocoupled product formed was reduced.

The aryl halides and reaction times for each run are listed in Table 18. All of the yields reported in Table 18 are of the heterocoupling product.

TABLE 18

Run	Aryl halide	Reaction time	Gas chromatography yield
a	Bromobenzene	3 hr.	100%
b	4-Bromotoluene <sup>a</sup>	6 hr.	93% <sup>b</sup>
c	Methyl-4-bromobenzoate	1 hr.	100%
d	4-Chloromethoxybenzene	17 hr.	19% <sup>c</sup>
e	4-Chlorotoluene <sup>d</sup>	4 hr.	29%
f	Methyl-4-chlorobenzoate	3 hr.	100%
g	4-Chlorobenzonitrile	2 hr.	100%

<sup>a</sup> A small amount of the homocoupled product was formed.

<sup>b</sup> 60 °C; 3 mmol of PhSi(OCH<sub>3</sub>)<sub>3</sub>

<sup>c</sup> Isolated yield

<sup>d</sup> Precipitation of Pd black was observed.

**EXAMPLE 21**

Reagents, analyses, and procedures were as described in Example 19, except that two heteroaryl halides were used. The heteroaryl halides and reaction times for each run are listed in Table 19. All of the yields reported in Table 19 are of the heterocoupling product.

**TABLE 19**

Run	Heteroaryl halide	Reaction time	Yield
a	2-Bromopyridine	7 hr.	81% <sup>a</sup>
b	2-Chloropyridine	7.5 hr.	81% <sup>b</sup>

<sup>a</sup> Isolated yield

<sup>b</sup> Gas chromatography yield

**EXAMPLE 22**

Reagents, analyses, and procedures were as described in Example 19, except as follows. Vinyltrimethoxysilane (2 mmol) was used instead of phenyltrimethoxysilane. Two different aryl halides (1.0 mmol each) were used. The aryl halide and reaction time for each run are listed in Table 20. The conversions reported in Table 20 are to the heterocoupling product.

**TABLE 20**

Run	Aryl halide	Reaction time	Conversion
a	4-Bromoacetophenone	8 hr.	100%
b	4-Chloroacetophenone	18 hr.	100%

**EXAMPLE 23**

Reagents, analyses, and procedures were as described in Example 19, except as follows. The metal compound was either Pd(CH<sub>3</sub>CO<sub>2</sub>)<sub>2</sub> (6.7mg, 0.03 mmol) or Pd<sub>2</sub>(dibenzylideneacetone)<sub>3</sub> (56.4mg, 0.03 mmol); and the N-heterocyclic carbene was 1,3-bis(2,6-diisopropylphenyl)imidazolinium chloride (13 mg, 0.03 mmol) or 1,3-bis(2,4,6-trimethylphenyl)imidazolinium chloride (10 mg, 0.03 mmol). Two phosphine ligands were also used. The amount of phenyltrimethoxysilane used in each run was different. The aryl halide used in all runs was 4-bromotoluene (1.0 mmol). The metal compound, ligand, temperature, amount of phenyltrimethoxysilane, and reaction time for each run are listed in Table 21. All



of the yields reported in Table 20 are of the heterocoupling product. --

TABLE 21

Run	Metal compound	Ligand	Amount of PhSi(OCH <sub>3</sub> ) <sub>3</sub>	T	Reaction time	GC yield
a	Pd <sub>2</sub> (dibenzylideneacetone) <sub>3</sub>	tri(cyclohexyl)phosphine	2 mmol	80 °C	1.5 hr.	100%
b	Pd <sub>2</sub> (dibenzylideneacetone) <sub>3</sub>	tri(o-tolyl)phosphine	2 mmol	80 °C	1 hr.	100%
c	Pd(CH <sub>3</sub> CO <sub>2</sub> ) <sub>2</sub>	1,3-bis(2,6-diisopropylphenyl)imidazolinium chloride	3 mmol	60 °C	6 hr.	93%
d	Pd(CH <sub>3</sub> CO <sub>2</sub> ) <sub>2</sub>	1,3-bis(2,4,6-trimethylphenyl)imidazolinium chloride	3 mmol	60 °C	2 hr.	60%

### Catalyst Systems of this Invention

The transition metal of the metal compound may be any of those in Groups 4-11 of the Periodic Table. For labeling of the groups of the Periodic Table, see for example, the Periodic Table appearing in *Chemical & Engineering News*, 1985, 69, 26. The metal compound can be in the form of an inorganic salt or an organic metal compound. Inorganic salts that can be used include the bromides, chlorides, fluorides, iodides, cyanides, nitrates, sulfides, sulfites, and sulfates. Organic metal compounds that may be used include complexes and salts such as the carboxylates, *e.g.*, the acetates or propionates, *etc.* Preferred are metals from Groups 8-11, especially ruthenium, osmium, rhodium, nickel, palladium, platinum, and copper. More preferred transition metals are the Group 10 metals, particularly nickel and palladium, and especially compounds in which the formal oxidation state of nickel or palladium is zero or two. Examples of ruthenium compounds are dichloro(1,5-cyclooctadiene)ruthenium, ruthenium acetate, ruthenium iodide, and the like. Osmium compounds that can be used include osmium chloride. Suitable rhodium compounds include bis(1,5-cyclooctadiene)rhodium trifluoromethanesulfonate and rhodium chloride. Suitable copper compounds include, but are not limited to, copper chloride, copper bromide, and copper cyanide. Suitable nickel compounds include bis(1,5-cyclooctadiene)nickel, nickel acetate, nickel oxalate, nickel phosphate, nickel stearate, nickel acetylacetonate, nickel tetrafluoroborate, nickel thiocyanate, nickel carbonate, and nickel sulfamate. Examples of palladium compounds include Pd(OAc)<sub>2</sub>, palladium(II) chloride, Pd(CH<sub>3</sub>CN)<sub>4</sub>(BF<sub>4</sub>)<sub>2</sub>, PdCl<sub>2</sub>(CH<sub>3</sub>CN)<sub>2</sub>, PdCl<sub>2</sub>(PhCN)<sub>2</sub>, PdCl<sub>2</sub>(PPh<sub>3</sub>)<sub>2</sub>, tris(dibenzylideneacetone)dipalladium(0)

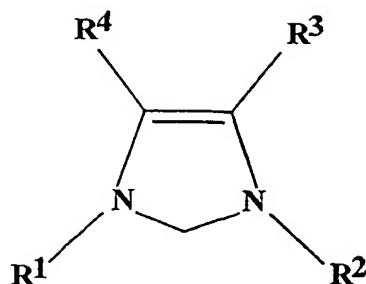
[which is also referred to herein as dipalladium tris(dibenzylideneacetone)], and palladium trifluoroacetate. Platinum compounds that can be used include platinum acetylacetonate and platinum chloride. More preferred are compounds of palladium. Palladium compounds such as palladium acetate and tris(dibenzylideneacetone)dipalladium(0) are most preferred.

For the imidazoline-2-ylidenes, imidazolidine-2-ylidenes, and their protonated salts, the aryl moiety of the aromatic group at the 1 and 3 positions can be, but is not limited to, phenyl, biphenyl, naphthyl, and anthracenyl. When the aryl moiety is not a phenyl group, the requirement for ortho substitution is fulfilled, for example, by a 1,3-disubstituted 2-naphthyl moiety (where the naphthyl group is bound to the nitrogen atom at the 2 position of the naphthyl group). Preferred as the aryl moiety is a phenyl group.

The secondary or tertiary group having at least three atoms at the ortho positions can be, for example, isopropyl, cyclopropyl, *sec*-butyl, *tert*-butyl, cyclobutyl, 3-pentyl, cyclopentyl, cyclohexyl, 2,5-dimethylhex-2-yl, norbornyl, and adamantyl. Preferably, the secondary or tertiary group has from three to about twelve carbon atoms, and more preferably has from three to about eight carbon atoms. Preferred groups are isopropyl and *tert*-butyl, especially isopropyl; preferably, both ortho groups are the same. Thus, preferred aromatic groups are 2,6-diisopropylphenyl, 2,6-di(*tert*-butyl)phenyl, and 2,4,6-triisopropylphenyl.

Examples of imidazoline-2-ylidenes include 1,3-bis(2,6-diisopropylphenyl)imidazoline, 1,3-bis(2-isopropyl-6-*tert*-butylphenyl)imidazoline, 1,3-bis(2,6-di-*tert*-butylphenyl)imidazoline, 1,3-bis(2,6-di(cyclohexyl)phenyl)imidazoline, 1,3-bis(2,4,6-triisopropylphenyl)imidazoline, 1,3-bis(2,6-dicyclopropylphenyl)imidazoline, 1,3-bis(2-isopropyl-6-cyclohexyl)phenyl)imidazoline, 1,3-bis(2,6-di-*tert*-butyl-4-methylphenyl)imidazoline, 1,3-bis(2,6-di(*sec*-butyl)phenyl)imidazoline, 1,3-bis(2,6-di-3-pentylphenyl)imidazoline, 1,3-bis(3-pentyl-6-cyclobutyl)phenyl)imidazoline, 1,3-bis(2,6-di(2,5-dimethylhex-2-yl)phenyl)imidazoline, and the like.

A highly preferred N-heterocyclic carbene is a protonated salt of an imidazoline-2-ylidene of the formula



wherein  $R^1$  and  $R^2$  are 2,6-diisopropylphenyl groups or 2,4,6-triisopropylphenyl groups, and  $R^3$  and  $R^4$  are each, independently, a hydrogen atom, a halogen atom, or a hydrocarbonyl group. Most preferably,  $R^3$  and  $R^4$  are both hydrogen atoms.

For the bis(imidazoline-2-ylidene)s, bis(imidazolidine-2-ylidene)s and their protonated salts, the bridging moiety can be selected from a large variety of moieties, including alkyl groups, aryl groups, and silyl groups, so long as the bridge has at least five atoms. Preferably, the bridge has five to about eight atoms. Atoms that can form the bridge include, but are not limited to, carbon, nitrogen, oxygen, silicon, and sulfur.

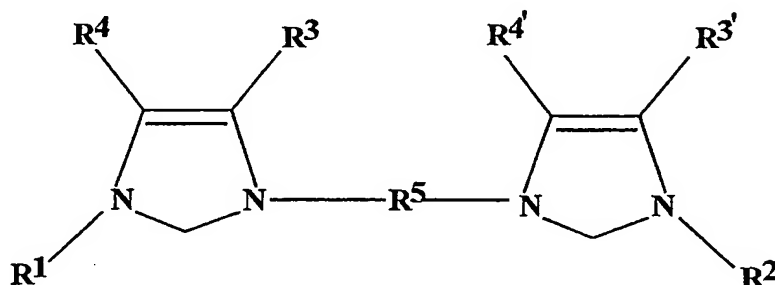
Examples of suitable bridging moieties include 1,5-pentylene, 1,6-hexylene, 1,5-hexylene, benzo ( $C_6H_4<$ ), substituted benzo, biphenylene, substituted biphenylene, binaphthylene, and substituted binaphthylene. Heterocyclic aromatic moieties such as, for example, pyridine, pyrimidine, pyrazine, pyridazine, furan, thiophene, oxathiolane, thianthrene, isobenzofuran, phenoxathiin, isothiazole, phenoxazine, and the like, can also form the bridge. The bridging moiety preferably is hydrocarbonylene. Preferably, the bridging moiety has from about eight to about thirty carbon atoms, and more preferably has from about ten to about twenty-five carbon atoms. Preferred bridging moieties include biphenylene, binaphthylene, and substituted benzo, with substituted benzo being more preferred. Highly preferred is benzo substituted with methyl groups.

The two nitrogen atoms that are not bound to the bridging moiety are each, independently, substituted by a secondary or tertiary group which has at least three atoms, preferably sterically bulky groups. Suitable groups include, but are not limited to, isopropyl, cyclopropyl, *sec*-butyl, *tert*-butyl, cyclobutyl, 3-pentyl, cyclopentyl, cyclohexyl, norbornyl,

2,5-dimethylhex-2-yl, adamantyl, tolyl, 3,5-dimethylphenyl, 2,4,6-trimethylphenyl, 2,6-diisopropylphenyl, 2,4,6-triisopropylphenyl, and 2,4,6-triisopropylphenylmethyl. Preferably, the secondary or tertiary group has from three to about twelve carbon atoms, and more preferably has from three to about eight carbon atoms. Preferably, both secondary or tertiary groups are the same. Preferred groups are *tert*-butyl, 2,4,6-trimethylphenyl, 2,6-*di**tert*-butylphenyl, 2,6-diisopropylphenyl, and 2,4,6-triisopropylphenyl. The 2,4,6-trimethylphenyl group is most preferred as the secondary or tertiary group for both of the nitrogen atoms that are not bound to the bridging moiety.

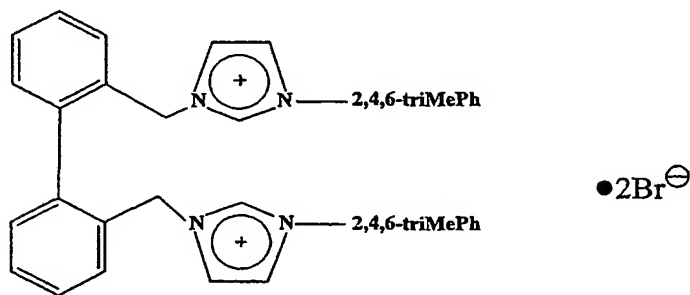
Examples of bis(imidazoline-2-ylidene)s include 3,3'-bis[3-(2,4,6-trimethylphenyl)imidazoline-2-ylidene]biphenyl and 2,7-bis[3-(2,6-diisopropylphenyl)imidazoline-2-ylidene]naphthalene.

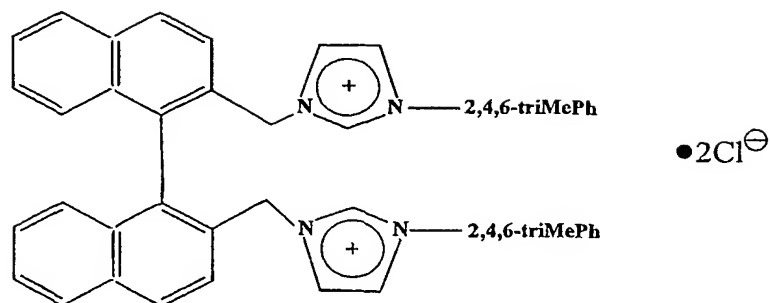
A highly preferred N-heterocyclic carbene is a protonated salt of a bis(imidazoline-2-ylidene) of the formula



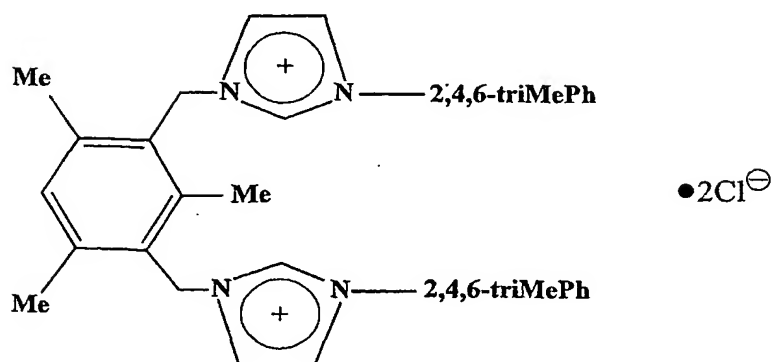
where  $R^1$  and  $R^2$  are 2,4,6-trimethylphenyl groups,  $R^3$ ,  $R^4$ ,  $R^{3'}$ ,  $R^{4'}$  are hydrogen atoms, and  $R^5$  is a biphenylene, binaphthylene, or substituted benzo moiety, and the bridge formed by the moiety has at least five atoms.

Particularly preferred protonated salts of bis(imidazoline-2-ylidene)s include





and



Without being bound by theory, it appears from thermochemical studies that the electron-donating ability of many of the imidazoline-2-ylidene carbene ligands is better than that of tri(cyclohexyl)phosphine and the steric demand of these carbene ligands is greater than that of tri(cyclohexyl)phosphine. This suggests that the N-heterocyclic carbene should possess steric bulk sufficient to stabilize both the free carbene and to stabilize reaction intermediates.

Imidazoline-2-ylidene carbenes and imidazolidine-2-ylidene carbenes are considerably less stable to air and moisture than their corresponding protonated imidazolinium and imidazolidinium salts. Thus, a highly preferred embodiment of this invention involves use of the corresponding imidazolinium salt to generate the imidazoline-2-ylidene *in situ* (similarly so for the imidazolidine-2-ylidene and the corresponding imidazolidinium salt) to form the catalyst system; this removes the need to handle the N-heterocyclic carbene ligands in an inert atmosphere. Protonated salts of the imidazoline-2-ylidene carbenes and

imidazolidine-2-ylidene carbenes are monoprotonated, while the protonated salts of the bis(imidazoline-2-ylidene)s and the bis(imidazolidine-2-ylidene)s are diprotonated. Suitable counterions for the protonated salts are virtually limitless, but halides are preferred counterions. The most preferred counterions are chloride and bromide. The imidazolinium salts are straightforward to synthesize and are air-stable. While the absence of oxygen is not necessary when using a protonated salt of an imidazoline-2-ylidene carbene or an imidazolidine-2-ylidene carbene, it is preferred. When using a neutral carbene, the absence of oxygen is necessary. In any instance where oxygen is excluded, the presence of an inert gas such as nitrogen, helium, or argon is preferred.

Often, a base is included when a protonated salt of an N-heterocyclic carbene is used. A large variety of strong bases are suitable for use in this invention with the protonated carbene salts. Generally, these are inorganic bases. Alkali metal salts are a preferred group of inorganic bases. Examples of suitable alkali metal salts include, but are not limited to, lithium carbonate, lithium *tert*-butoxide, sodium bicarbonate, sodium carbonate, sodium *tert*-butoxide, sodium oxide, sodium tetrafluoroborate, potassium acetate, potassium carbonate, potassium fluoride, potassium *tert*-butoxide, potassium nitrite, potassium phosphate, potassium sulfite, potassium hexafluorophosphate, cesium acetate, cesium bicarbonate, cesium carbonate, cesium fluoride, cesium nitrate, and cesium sulfate. Alkali metal salts of carboxylic acid anions (*e.g.*, acetate, trifluoroacetate, citrate, formate, oxalate, propionate, tartrate, *etc.*) are also suitable for use as the inorganic base in this invention. More preferred are salts of potassium and cesium. Choice(s) of inorganic base will vary with the particular catalyst system involved. Amine bases have been observed to poison the catalyst system of the invention in some instances, and thus are not preferred.

While not necessary when using protonated salts of N-heterocyclic carbenes, the absence of oxygen and water is preferred when forming the catalyst systems of this invention. Conversely, the exclusion of oxygen and water is generally necessary when neutral carbenes are used. The presence of an inert gas such as argon or nitrogen is preferred when oxygen and/or water are excluded.

Normally, the molar ratio of metal atoms of the metal compound to N-heterocyclic carbene molecules is in the range of from about 1:0.5 to about 1:5, and more preferably in the range of from about 1:1 to about 1:3. When a base is included with the catalyst system of this

invention, the base is preferably used in excess.

The following examples are presented for purposes of illustration, and are not intended to impose limitations on the scope of this embodiment of the invention.

## EXAMPLES 24-28

### GENERAL PROCEDURES

**Reagents.** All aryl chlorides (Aldrich Chemical Company), phenylboronic acid (Aldrich), N-methylamine (Aldrich), phenylmagnesium bromide (1.0 moles per liter in tetrahydrofuran; Aldrich), KO<sup>t</sup>Bu (Aldrich), Cs<sub>2</sub>CO<sub>3</sub> (Aldrich), and Pd<sub>2</sub>(dibenzylideneacetone)<sub>3</sub> (Strem Chemical Company) were used as received. 1,4-Dioxane was either distilled from Na/benzophenone ketyl or purchased (anhydrous, Aldrich). Flash chromatography was performed on silica gel 60 (230-400 mesh; Natland International Corporation).

1,3-bis(2,4,6-trimethylphenyl)imidazoline-2-ylidene and 1,3-Bis(2,4,6-trimethylphenyl)imidazolinium chloride were prepared according to reported procedures in U.S. Patent No. 5,077,414, and/or Arduengo, A. J. III., Dias, H.V.R.; Harlow, R.L. and Kline, M. *J. Am. Chem. Soc.*, 1992, **114**, 5530-5534. The synthesis of 1,3-bis(2,6-diisopropylphenyl)imidazolinium chloride was carried out in a similar fashion, except that it was done in two steps rather than in one pot (see Example 1).

**Analyses.** All reactions were monitored by thin layer chromatography (TLC). <sup>1</sup>H and <sup>13</sup>C nuclear magnetic resonance (NMR) spectra were recorded on a 300 MHz NMR spectrometer (Varian, Incorporated) or 400 MHz NMR spectrometer (Varian) at ambient temperature in CDCl<sub>3</sub> (Cambridge Isotope Laboratories, Incorporated).

**Conditions.** All reactions were carried out under an atmosphere of argon in oven-dried glassware with magnetic stirring, unless otherwise indicated.

### EXAMPLE 24

2,6-Diisopropylaniline (100g, 0.56 mol), glyoxal (31.5 mL, 40% in water, 0.28 mol), and absolute ethanol (500 mL) were charged to a round-bottom flask. A few drops of formic acid were added, and the solution immediately changed from colorless to yellow. After a few hours, a yellow precipitate appeared. The reaction mixture was stirred for another two days.

The yellow precipitate was collected by filtration and washed with cold methanol. 1,4-Bis(2,6-diisopropylphenyl)diazabutadiene was obtained in the amount of 81.74g, a yield of 77.5%.

Toluene (500 mL) and 1,4-Bis(2,6-diisopropylphenyl)diazabutadiene (25g, 66 mol) were added to a reaction vessel, followed by solid paraformaldehyde (2.0g, 66 mmol). The reaction mixture was heated to 100°C until most of the paraformaldehyde had dissolved. The mixture was then cooled to 40°C, and HCl (16.5mL, 4 moles per liter in dioxane, 66 mmol) was added via syringe. The reaction mixture turned brown in color, and a white precipitate appeared after a few hours. The reaction mixture was stirred at room temperature for another 36 hours. The precipitate was then collected by filtration and washed with tetrahydrofuran. The yield of 1,3-bis(2,6-diisopropylphenyl)imidazolinium chloride was 13.1g, or 47%.

Imidazolidine-2-ylidenes can be prepared by hydrogenation of the corresponding imidazolinium salt, for example, with KH in tetrahydrofuran. See in this connection Arduengo et al., *J. Am. Chem. Soc.*, 1995, 117, 11027.

#### EXAMPLE 25

Catalyzed amination reactions were carried out using several different imidazolinium-2-ylidene chlorides. For each run, a Schlenk tube was charged with Pd<sub>2</sub>(dibenzylideneacetone)<sub>3</sub> (10 mg, 0.01 mmol), 1,3-bis(substituted)imidazolinium chloride (0.04 mmol), and a magnetic stirring bar. After a 30 minute catalyst activation period, 1,4-dioxane (3 mL), KO<sup>t</sup>Bu (168mg, 1.5 mmol), 4-chlorotoluene (1.0 mmol), and N-methylaniline (1.2 mmol) were added in turn to the Schlenk tube. The Schlenk tube was placed in a 100°C oil bath and the mixture was stirred for 3 hours. The mixture was then allowed to cool to room temperature. The mixture was washed with diethyl ether. The organic layer and the diethyl ether extracts were combined, washed with saturated saline solution, and then dried over MgSO<sub>4</sub>. The solvent was removed under vacuum and the residue was purified by flash chromatography using hexane or a mixture of hexane and ethyl acetate.

The 1,3-bis(substituted)imidazolinium chloride used in each run are listed in Table 22. All of the yields reported in Table 22 are of the heterocoupling product, and are the average of two runs.



TABLE 22

Run	1,3-Bis(substituted)imidazolinium chloride	Isolated yield
A	None	0
B	1,3-Bis( <i>p</i> -tolyl)imidazolinium chloride	<5%
C	1,3-Bis(2,6-dimethylphenyl)imidazolinium chloride	11%
D	1,3-Bis(2,4,6-trimethylphenyl)imidazolinium chloride	22%
E	1,3-Bis(2,6-diisopropylphenyl)imidazolinium chloride	98%

It can be seen that as the steric bulk of the groups bound to the nitrogen atom increases, so does the yield of the reaction. A significant improvement in yield is observed when the ortho methyl groups (Run D) are replaced by isopropyl groups (Run E).

## EXAMPLE 26

Catalyzed Kumada coupling reactions were carried out in a variety of solvents and/or solvent mixtures. For each run, a Schlenk tube was charged with Pd<sub>2</sub>(dibenzylideneacetone)<sub>3</sub> (10 mg, 0.01 mmol), 1,3-bis(substituted)imidazolinium chloride (0.04 mmol), and a magnetic stirring bar. After a 30 minute catalyst activation period, solvent (5 mL), 4-chlorotoluene (1.0 mmol), and phenylmagnesium bromide (1.2 mmol) were added in turn to the Schlenk tube. The Schlenk tube was placed in an oil bath and the mixture was heated and stirred for a number of hours. The mixture was then allowed to cool to room temperature. The mixture was hydrolyzed either with aqueous HCl (1.0 moles per liter) or H<sub>4</sub>NCl solution. The solvent was removed under vacuum and the residue was purified by flash chromatography using hexane or a mixture of hexane and ethyl acetate.

The 1,3-bis(substituted)imidazolinium chloride used in each run are listed in Table 23. All of the yields reported in Table 23 are of the heterocoupling product, and are the average of two runs.

TABLE 23

Run	1,3-bis(substituted)imidazolinium chloride	Solvent	T	Reaction time	Isolated yield
a	1,3-Bis(2,4,6-trimethylphenyl)-imidazolinium chloride	Et <sub>2</sub> O/THF	45°C	20 hr.	35%
b	1,3-Bis(2,6-diisopropylphenyl)-imidazolinium chloride	Et <sub>2</sub> O/THF	45°C	20 hr.	97%

c	1,3-Bis(2,6-diisopropylphenyl)-imidazolinium chloride	toluene/THF	80°C	20 hr.	10%
d	1,3-Bis(2,6-diisopropylphenyl)-imidazolinium chloride	THF	80°C	5 hr.	86%
e	None	dioxane/THF	80°C	3 hr.	0
f	1,3-Bis(2,4,6-trimethylphenyl)-imidazolinium chloride	dioxane/THF	80°C	3 hr.	41%
g	1,3-Bis(2,6-diisopropylphenyl)-imidazolinium chloride	dioxane/THF	80°C	3 hr.	99%

Comparison of the results in Table 23 clearly shows that, for each solvent or solvent mixture, significantly better yields are obtained with 1,3-bis(2,6-diisopropylphenyl)imidazolinium chloride, the N-heterocyclic carbene which has secondary groups at the ortho positions of the aromatic rings of the nitrogen-bound groups.

#### EXAMPLE 27

Six bis(imidazolinium) salts (see Table 24) were prepared by heating the dibromide or dichloride of the molecule intended to be the bridging moiety with two equivalents of an 1-aryl-imidazol in xylene. As an example, a mixture of dibromomethane (1.0 mmol) and N-(3,5-dimethylphenyl)imidazoline (2.0 mmol) was heated in xylene (5 mL) at 140°C for 2 days. This afforded the salt shown in Run B of Table 3 in 70% yield. Alternatively, a mixture of 1,3-di( $\alpha$ -chloromethyl)-2,4,6-trimethylbenzene (1.0 mmol) and N-(2,4,6-trimethylphenyl)imidazoline (2.0 mmol) was heated in xylene (5 mL) at 120°C for 48 hours and furnished the salt shown in Run F of Table 24 in 85% yield.

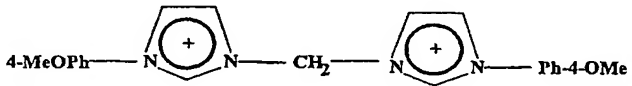
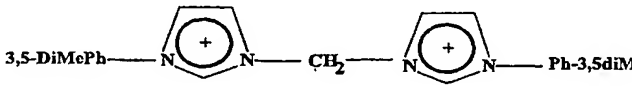
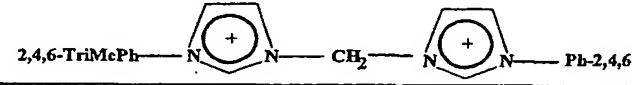
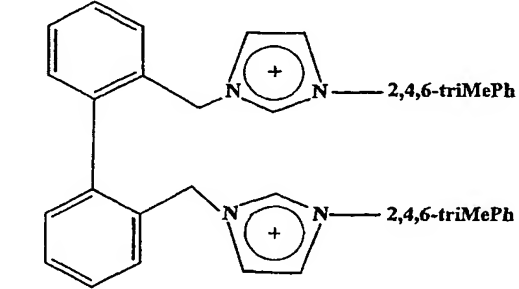
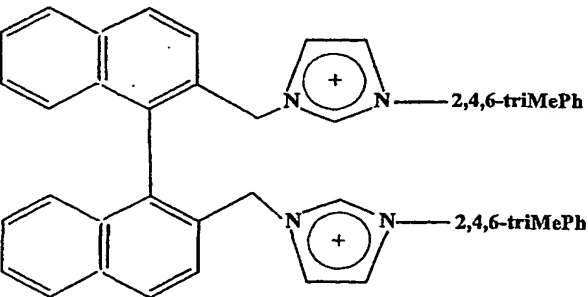
Bis(imidazolidine-2-ylidene)s can be prepared by hydrogenation of the corresponding imidazolinium salt, for example, with KH in tetrahydrofuran. See in this connection Arduengo et al., *J. Am. Chem. Soc.*, 1995, 117, 11027.

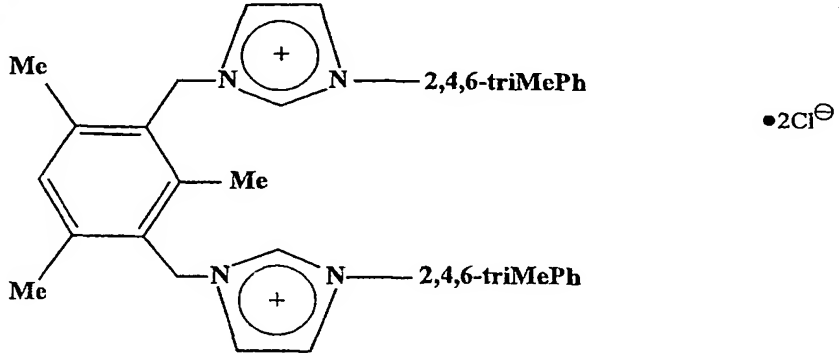
#### EXAMPLE 28

Catalyzed Suzuki coupling reactions were carried out using several different bis(imidazolinium-2-ylidene) salts. The procedure used in all runs of this example are as follows. A Schlenk tube was charged with Pd(CH<sub>3</sub>CO<sub>2</sub>)<sub>2</sub> (5.6 mg, 0.025 mmol), one of the bis(imidazolinium-2-ylidene) salts prepared in Example 27 (0.025 mmol), Cs<sub>2</sub>CO<sub>3</sub> (2.00 equivalents), and a magnetic stirring bar. After a 30 minute catalyst activation period,

1,4-dioxane (3 mL), 4-chlorotoluene (1.0 mmol), and phenylboronic acid (1.5 mmol) were added in turn to the Schlenk tube. The Schlenk tube was placed in a 80°C oil bath and stirred for a number of hours. The mixture was then allowed to cool to room temperature. The bis(imidazoline-2-ylidene) salt used in each run is listed in Table 24. All of the yields reported in Table 24 are of the heterocoupling product, and are the average of two runs.

TABLE 24

Run	Bis(imidazolium) salt	Reaction time	Isolated yield
A		24 hr.	trace <sup>a</sup>
B		24 hr.	<5% <sup>a</sup>
C		6 hr.	32% <sup>a</sup>
D		4 hr.	65% <sup>a</sup>
E		4 hr.	87%

F		1.5 hr.	99%
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<sup>a</sup>4-Chlorotoluene was not completely consumed and precipitation of Pd black was observed.

The data in Table 24 clearly demonstrate that dramatically improved yields are obtained in shorter reaction times when the bis(imidazoline-2-ylidene) salt has a bridge of five or more atoms (Runs D-F).

It is to be understood that the reactants and components referred to by chemical name or formula anywhere in the specification or claims hereof, whether referred to in the singular or plural, are identified as they exist prior to coming into contact with another substance referred to by chemical name or chemical type (*e.g.*, another reactant, a solvent, *etc.*). It matters not what preliminary chemical changes, transformations and/or reactions, if any, take place in the resulting mixture or solution or reaction medium as such changes, transformations and/or reactions are the natural result of bringing the specified reactants and/or components together under the conditions called for pursuant to this disclosure. Thus the reactants and components are identified as ingredients to be brought together in connection with performing a desired chemical reaction or in forming a mixture to be used in conducting a desired reaction. Accordingly, even though the claims hereinafter may refer to substances, components and/or ingredients in the present tense ("comprises", "is", *etc.*), the reference is to the substance, component or ingredient as it existed at the time just before it was first contacted, blended or mixed with one or more other substances, components and/or ingredients in accordance with the present disclosure. Whatever transformations, if any, that occur *in situ* as a reaction is conducted is what the claim is intended to cover. Thus the fact that a substance, component or ingredient may have lost its original identity through a chemical reaction or transformation during the course of contacting, blending or mixing operations, if conducted in accordance with this disclosure and with the application of

common sense and the ordinary skill of a chemist, is thus wholly immaterial for an accurate understanding and appreciation of the true meaning and substance of this disclosure and the claims thereof.

Each and every patent or other publication referred to in any portion of this specification is incorporated *in toto* into this disclosure by reference, as if fully set forth herein.

This invention is susceptible to considerable variation in its practice. Therefore the foregoing description is not intended to limit, and should not be construed as limiting, the invention to the particular exemplifications presented hereinabove. Rather, what is intended to be covered is as set forth in the ensuing claims and the equivalents thereof permitted as a matter of law.

## CLAIMS

1. A process which comprises mixing, in a liquid medium,
- i) at least one strong base;
  - ii) at least one aryl halide or aryl pseudohalide, wherein the aryl halide or aryl pseudohalide has, directly bonded to the aromatic ring(s), at least one halogen atom selected from the group consisting of a chlorine atom, a bromine atom, and an iodine atom;
  - iii) at least one transmetalating agent selected from the group consisting of at least one arylboronic acid in which all substituents are other than chlorine atoms, bromine atoms, iodine atoms, or pseudohalide groups; at least one primary amine and/or at least one secondary amine; at least one Grignard reagent; at least one organotin compound wherein the tin atom is quaternary, wherein one group bound to the tin atom is unsaturated at the alpha or beta position, and wherein each of the remaining groups bound to the tin atom is a saturated group; and at least one silane wherein the silicon atom is quaternary, wherein one group bound to the silicon atom is unsaturated at the alpha or beta position, and wherein each of the remaining groups bound to the silicon atom is a saturated hydrocarbyl or a saturated hydrocarbyloxy group; all with the proviso that (A) if the transmetalating agent is the arylboronic acid, all substituents of the aryl halide or aryl pseudohalide are other than boronic acid groups, (B) if the transmetalating agent is the primary and/or secondary amine, all substituents of the aryl halide or aryl pseudohalide are other than amino groups, (C) if the transmetalating agent is at least one Grignard reagent, the process is carried out with the exclusion of water and the strong base is optional, (D) if the transmetalating agent is the organotin compound, all substituents of the aryl halide or aryl pseudohalide are other than stannyl groups, and (E) if the transmetalating agent is the silane, all substituents of the aryl halide or aryl pseudohalide are other than silyl groups;
  - iv) at least one metal compound comprising at least one metal atom selected from nickel, palladium, and platinum, wherein the formal oxidation state of the metal is zero or two; and
  - v) at least one N-heterocyclic carbene selected from the group consisting of an imidazoline-2-ylidene wherein the 1 and 3 positions are each, independently,

substituted by a secondary or tertiary group which has at least three atoms, or a protonated salt thereof; an imidazolidine-2-ylidene wherein the 1 and 3 positions are each, independently, substituted by a secondary or tertiary group which has at least three atoms, or a protonated salt thereof; a bis(imidazoline-2-ylidene) wherein a bridging moiety is bound to one nitrogen atom of each ring, and wherein the remaining two nitrogen atoms are each, independently, substituted by a secondary or tertiary group which has at least three atoms, or a protonated salt thereof; and a bis(imidazolidine-2-ylidene) wherein a bridging moiety is bound to one nitrogen atom of each ring, and wherein the remaining two nitrogen atoms are each, independently, substituted by a secondary or tertiary group which has at least three atoms, or a protonated salt thereof; and mixtures of two or more of the foregoing.

2. A process according to Claim 1 wherein said transmetalating agent is at least one arylboronic acid in which all substituents are other than chlorine atoms, bromine atoms, iodine atoms, or pseudohalide groups.

3. A process according to Claim 2 wherein said aryl halide or aryl pseudohalide is 4-methylphenyltoluenesulfonate.

4. A process according to Claim 2 wherein said arylboronic acid is a phenylboronic acid.

5. A process according to Claim 4 wherein said phenylboronic acid is selected from the group consisting of 2-methylphenylboronic acid, 4-methylphenylboronic acid, 4-methoxyphenylboronic acid, and phenylboronic acid.

6. A process according to Claim 2 wherein said arylboronic acid is a naphthylboronic acid.

7. A process according to Claim 6 wherein said naphthylboronic acid is 6-methoxy-2-naphthylboronic acid.

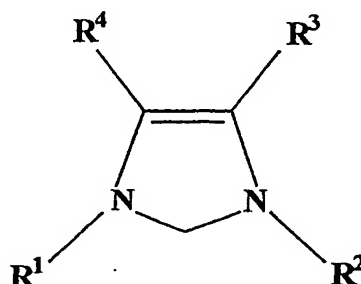
8. A process according to Claim 2 wherein said strong base is an alkali metal salt selected from the group consisting of potassium carbonate, potassium tert-butoxide, and cesium carbonate.

9. A process according to Claim 2 wherein said strong base is cesium carbonate, wherein the metal compound is selected from the group consisting of palladium acetate, palladium chloride, and dipalladium tris(dibenzylideneacetone), and wherein the aryl halide

or aryl pseudohalide is an aryl chloride.

10. A process according to Claim 2 wherein said strong base is either potassium carbonate or cesium carbonate, wherein the metal compound is selected from the group consisting of palladium acetate, palladium chloride, and dipalladium tris(dibenzylideneacetone), and wherein the aryl halide or aryl pseudohalide is either an aryl trifluoromethanesulfonate or an aryl toluenesulfonate.

11. A process according to Claim 2 wherein said N-heterocyclic carbene is a protonated salt of an imidazoline-2-ylidene of the formula



wherein

R<sup>1</sup> and R<sup>2</sup> are the same, and each is either a 2,4,6-trimethylphenyl group or a 2,6-diisopropylphenyl group, and

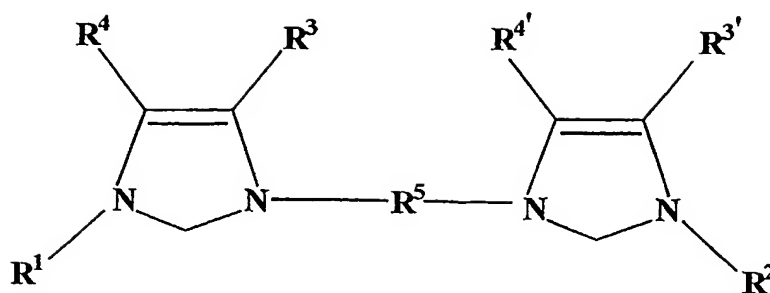
R<sup>3</sup> and R<sup>4</sup> are each, independently, a hydrogen atom, a halogen atom, or a hydrocarbyl group,

and wherein said strong base is a cesium salt and said metal compound is a palladium compound.

12. A process according to Claim 11 wherein said cesium salt is cesium carbonate and wherein said palladium compound is selected from the group consisting of palladium acetate, palladium chloride, and dipalladium tris(dibenzylideneacetone).

13. A process according to Claim 2 wherein said N-heterocyclic carbene is a protonated salt of a bis(imidazoline-2-ylidene) of the formula





wherein

$R^1$  and  $R^2$  are the same, and each is either a 2,4,6-trimethylphenyl group or a 2,6-diisopropylphenyl group, and

$R^3$  and  $R^4$  are each, independently, a hydrogen atom, a halogen atom, or a hydrocarbyl group,

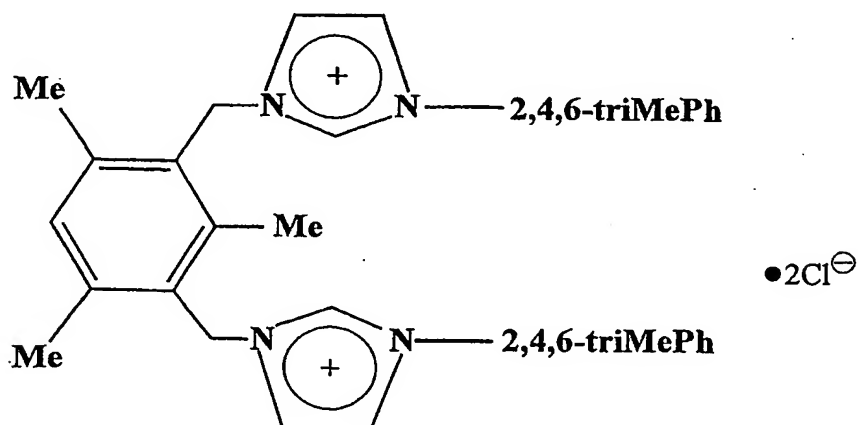
$R^{3'}$  and  $R^{4'}$  are as defined for  $R^3$  and  $R^4$ , and

$R^5$  is a bridging group that links the two imidazoline rings,

and wherein said strong base is a cesium salt and said metal compound is a palladium compound.

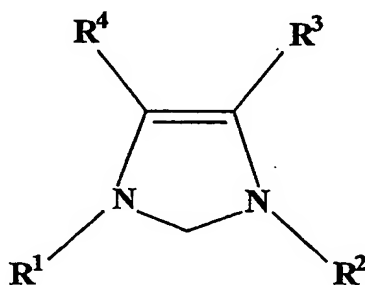
14. A process according to Claim 13 wherein said cesium salt is cesium carbonate and wherein said palladium compound is palladium acetate.

15. A process according to Claim 2 wherein said N-heterocyclic carbene is



16. A process according to Claim 1 wherein said transmetalating agent is at least one primary amine and/or at least one secondary amine.

17. A process according to Claim 16 wherein said aryl halide is 4-bromotoluene.
18. A process according to Claim 16 wherein said aryl halide or aryl pseudohalide is bromobenzene.
19. A process according to Claim 16 wherein said aryl halide or aryl pseudohalide is 1-bromonaphthalene.
20. A process according to Claim 16 wherein said amine is a primary amine.
21. A process according to Claim 20 wherein said primary amine is either aniline or hexylamine.
22. A process according to Claim 16 wherein said amine is a secondary amine.
23. A process according to Claim 22 wherein said secondary amine is selected from the group consisting of di-n-butylamine, piperidine, and N-methylaniline.
24. A process according to Claim 16 wherein said amine is a naphthylamine.
25. A process according to Claim 24 wherein said naphthylamine is 6-methoxy-2-naphthylamine.
26. A process according to Claim 16 wherein said strong base is potassium tert-butoxide, wherein the metal compound is selected from the group consisting of palladium acetate, palladium chloride, and dipalladium tris(dibenzylideneacetone), and wherein the aryl halide or aryl pseudohalide is an aryl chloride.
27. A process according to Claim 16 wherein said strong base is either potassium carbonate or potassium tert-butoxide, wherein the metal compound is selected from the group consisting of palladium acetate, palladium chloride, and dipalladium tris(dibenzylideneacetone), and wherein the aryl halide or aryl pseudohalide is either an aryl trifluoromethanesulfonate or an aryl toluenesulfonate.
28. A process according to Claim 16 wherein said N-heterocyclic carbene is an imidazoline-2-ylidene of the formula



or a protonated salt thereof, wherein

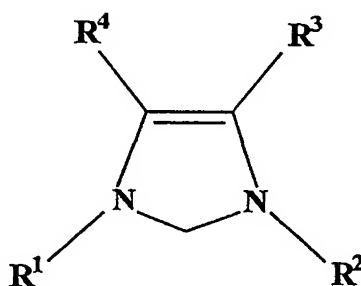
$R^1$  and  $R^2$  are the same, and each is either a 2,4,6-trimethylphenyl group or a 2,6-diisopropylphenyl group, and

$R^3$  and  $R^4$  are each, independently, a hydrogen atom, a halogen atom, or a hydrocarbyl group,

and wherein said strong base is a potassium salt and wherein said metal compound is a palladium compound.

29. A process according to Claim 28 wherein said potassium salt is potassium tert-butoxide, and wherein said palladium compound is selected from the group consisting of palladium acetate, palladium chloride, and dipalladium tris(dibenzylideneacetone).

30. A process according to Claim 16 wherein said N-heterocyclic carbene is an imidazoline-2-ylidene of the formula



or a protonated salt thereof, wherein

$R^1$  and  $R^2$  are the same, and each is either a 2,4,6-trimethylphenyl group or a 2,6-diisopropylphenyl group, and

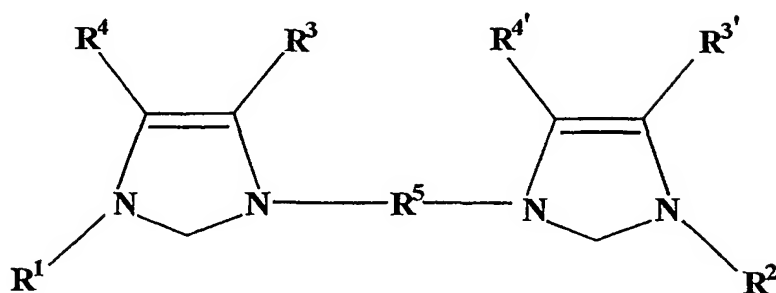
$R^3$  and  $R^4$  are each, independently, a hydrogen atom, a halogen atom, or a hydrocarbyl group,

and wherein said strong base is a potassium salt and said metal compound is a palladium compound.

31. A process according to Claim 30 wherein said potassium salt is potassium tert-butoxide, and wherein said palladium compound is selected from the group consisting of palladium acetate, palladium chloride, and dipalladium tris(dibenzylideneacetone).

32. A process according to Claim 16 wherein said N-heterocyclic carbene is a

protonated salt of a bis(imidazoline-2-ylidene) of the formula



wherein

$R^1$  and  $R^2$  are the same, and each is selected from the group consisting of a 2,4,6-trimethylphenyl group, a 2,6-diisopropylphenyl group and a 2,4,6-triisopropylphenyl group, and

$R^3$  and  $R^4$  are each, independently, a hydrogen atom, a halogen atom, or a hydrocarbyl group,

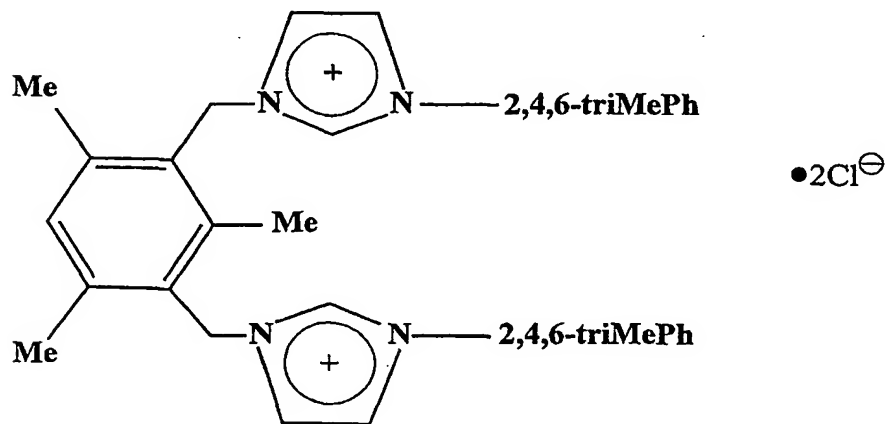
$R^{3'}$  and  $R^{4'}$  are as defined for  $R^3$  and  $R^4$ , and

$R^5$  is a bridging group that links the two imidazoline rings,

and wherein said strong base is a potassium salt and said metal compound is a palladium compound.

33. A process according to Claim 32 wherein said potassium salt is potassium tert-butoxide, and wherein said palladium compound is palladium acetate.

34. A process according to Claim 16 wherein said N-heterocyclic carbene is



35. A process according to Claim 16 wherein the molar ratio of aryl halide or aryl

pseudohalide to amine is in the range of from about 1:1 to about 1:3.

36. A process according to Claim 1 wherein said aryl halide or aryl pseudohalide is an aryl halide, and said transmetalating agent is at least one Grignard Reagent.

37. A process according to Claim 36 wherein said liquid medium comprises tetrahydrofuran.

38. A process according to Claim 36 wherein said liquid medium comprises a mixture of two or more ethers.

39. A process according to Claim 36 wherein said aryl halide is aryl chloride.

40. A process according to Claim 39 wherein said aryl chloride is selected from the group consisting of 4-chlorotoluene, 1-methoxy-4-chlorobenzene, 1,4-dimethyl-2-chlorobenzene, and methyl-4-chlorobenzoate.

41. A process according to Claim 36 wherein said aryl halide is either 4-bromotoluene or methyl-4-bromobenzoate.

42. A process according to Claim 36 wherein said aryl halide is a phenyl halide.

43. A process according to Claim 42 wherein said phenyl halide is chlorobenzene.

44. A process according to Claim 36 wherein said aryl halide is a naphthyl halide.

45. A process according to Claim 44 wherein said naphthyl halide is either 1-bromonaphthalene or 6-methoxy-2-bromonaphthalene.

46. A process according to Claim 36 wherein said Grignard reagent is a phenylmagnesium halide.

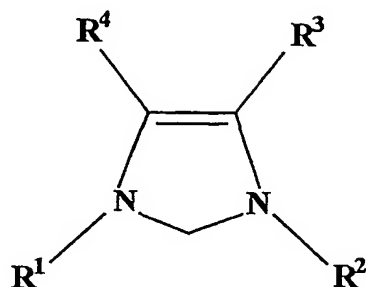
47. A process according to Claim 46 wherein said phenylmagnesium halide is selected from the group consisting of 2-fluorophenylmagnesium bromide, 3-methylphenylmagnesium bromide, 4-methylphenylmagnesium bromide, 2,4,6-trimethylphenylmagnesium bromide, and phenylmagnesium bromide.

48. A process according to Claim 36 wherein said Grignard reagent is a naphthylmagnesium halide.

49. A process according to Claim 48 wherein said naphthylmagnesium halide is either 6-methoxy-2-naphthylmagnesium bromide or 1-naphthylmagnesium bromide.

50. A process according to Claim 36 wherein the metal compound is selected from the group consisting of palladium acetate, palladium chloride, and dipalladium tris(dibenzylideneacetone), and wherein the aryl halide is an aryl chloride.

51. A process according to Claim 36 wherein said N-heterocyclic carbene is an imidazoline-2-ylidene of the formula



or a protonated salt thereof, wherein

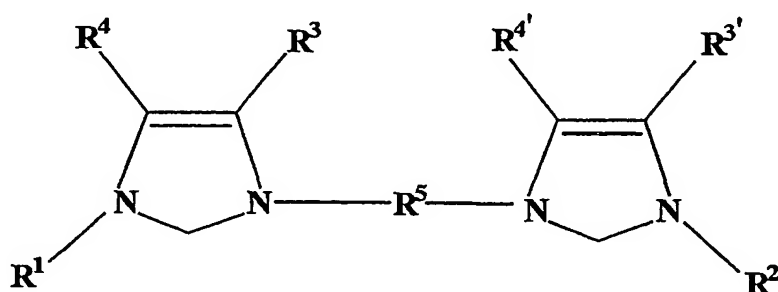
$R^1$  and  $R^2$  are the same, and each is either a 2,4,6-trimethylphenyl group or a 2,6-diisopropylphenyl group, and

$R^3$  and  $R^4$  are each, independently, a hydrogen atom, a halogen atom, or a hydrocarbyl group,

and wherein said metal compound is a palladium compound.

52. A process according to Claim 51 wherein said palladium compound is selected from the group consisting of palladium acetate, palladium chloride, and dipalladium tris(dibenzylideneacetone).

53. A process according to Claim 36 wherein said N-heterocyclic carbene is a protonated salt of a bis(imidazoline-2-ylidene) of the formula



wherein

$R1$  and  $R2$  are the same, and each is selected from the group consisting of a 2,4,6-trimethylphenyl group, a 2,6-diisopropylphenyl group and a 2,4,6-triisopropylphenyl group,

R3 and R4 are each, independently, a hydrogen atom, a halogen atom, or a hydrocarbyl group,

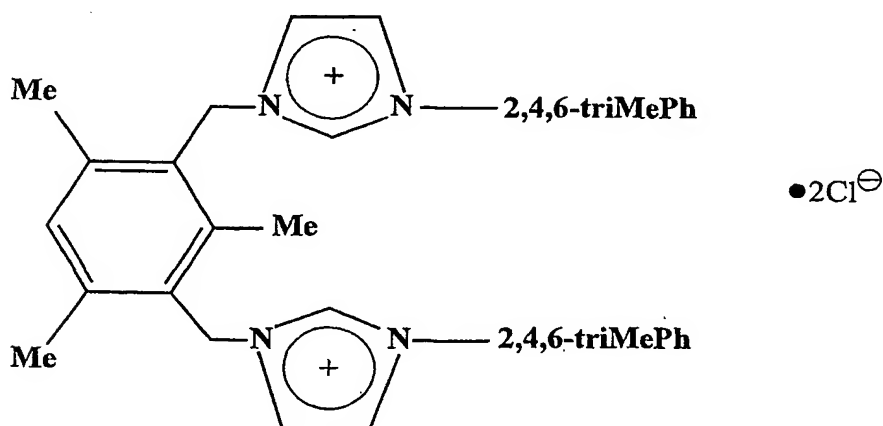
R3' and R4' are as defined for R3 and R4, and

R5 is a bridging group that links the two imidazoline rings,

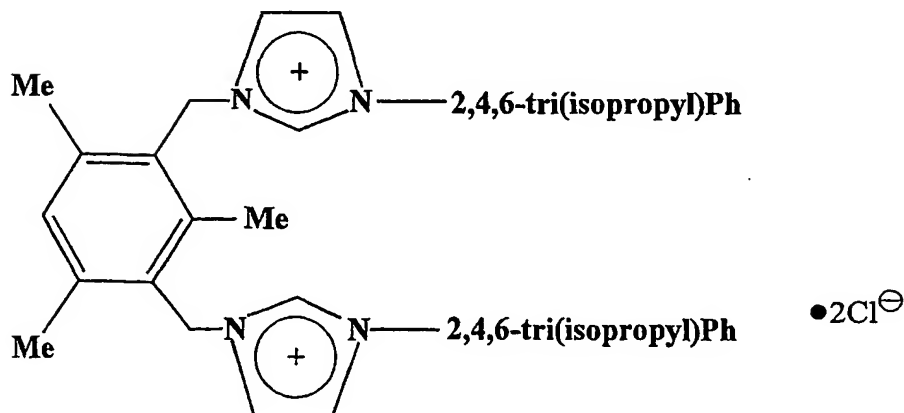
and wherein said metal compound is a palladium compound.

54. A process according to Claim 53 wherein said palladium compound is palladium acetate.

55. A process according to Claim 36 wherein said N-heterocyclic carbene is either



or



56. A process according to Claim 36 wherein the molar ratio of aryl halide to Grignard reagent is in the range of from about 1:1 to about 1:5.

57. A process according to Claim 36 wherein said aryl halide is an aryl chloride, and wherein the temperature is in the range of from about 40°C to about 150°C.

58. A process according to Claim 36 wherein said aryl halide is either an aryl bromide or an aryl iodide, and wherein the temperature is in the range of from about 20°C to about 70°C.

59. A process according to Claim 1 wherein said transmetalating agent is at least one organotin compound wherein the tin atom is quaternary, wherein one group bound to the tin atom is unsaturated at the alpha or beta position, and wherein each of the remaining groups bound to the tin atom is a saturated group.

60. A process according to Claim 59 wherein said aryl halide or aryl pseudohalide is selected from the group consisting of 4-chlorotoluene, 1-methoxy-4-chlorobenzene, 1,4-dimethyl-2-chlorobenzene, and methyl-4-chlorobenzoate.

61. A process according to Claim 59 wherein said unsaturated group of the organotin compound is a phenyl group.

62. A process according to Claim 61 wherein said organotin compound is either phenyl(trimethyl)tin or phenyl(trin-butyl)tin.

63. A process according to Claim 59 wherein said unsaturated group of the organotin compound is a naphthyl group.

64. A process according to Claim 63 wherein said naphthyl group is a 6-methoxy-2-naphthyl group.

65. A process according to Claim 59 wherein said unsaturated group of the organotin compound is a vinyl group.

66. A process according to Claim 65 wherein said organotin compound is either trimethyl(vinyl)tin or trin-butyl(vinyl)tin.

67. A process according to Claim 59 wherein said unsaturated group of the organotin compound is an allyl group.

68. A process according to Claim 67 wherein said organotin compound is either (allyl)trimethyltin or (allyl)trin-butyltin.

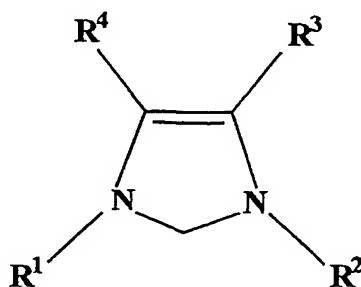
69. A process according to Claim 59 wherein said strong base is cesium fluoride, wherein the metal compound is selected from the group consisting of palladium acetate, palladium chloride, and dipalladium tris(dibenzylideneacetone), and wherein the aryl halide



or aryl pseudohalide is an aryl chloride.

70. A process according to Claim 59 wherein said strong base is either potassium fluoride or cesium fluoride, wherein the metal compound is selected from the group consisting of palladium acetate, palladium chloride, and dipalladium tris(dibenzylideneacetone), and wherein the aryl halide or aryl pseudohalide is either an aryl trifluoromethanesulfonate or an aryl toluenesulfonate.

71. A process according to Claim 59 wherein said N-heterocyclic carbene is an imidazoline-2-ylidene of the formula



or a protonated salt thereof, wherein

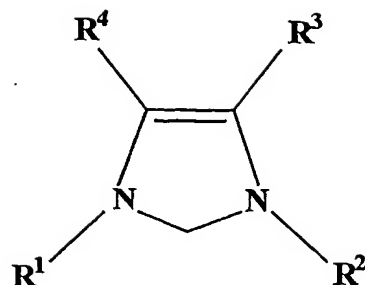
R<sup>1</sup> and R<sup>2</sup> are the same, and each is either a 2,4,6-trimethylphenyl group or a 2,6-diisopropylphenyl group, and

R<sup>3</sup> and R<sup>4</sup> are each, independently, a hydrogen atom, a halogen atom, or a hydrocarbyl group,

and wherein said strong base is a cesium salt and wherein said metal compound is a palladium compound.

72. A process according to Claim 71 wherein said cesium salt is cesium fluoride and wherein said palladium compound is selected from the group consisting of palladium acetate, palladium chloride, and dipalladium tris(dibenzylideneacetone).

73. A process according to Claim 59 wherein said N-heterocyclic carbene is an imidazoline-2-ylidene of the formula



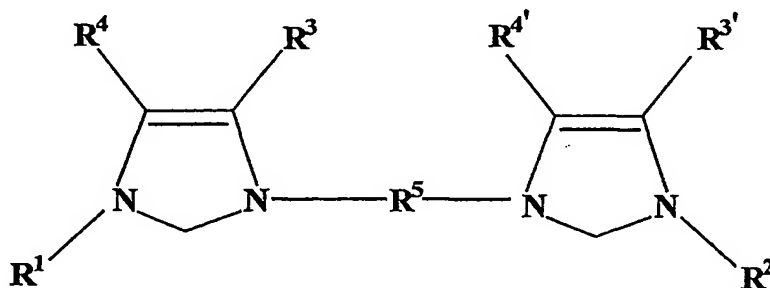
or a protonated salt thereof, wherein

$R^1$  and  $R^2$  are the same, and each is either a 2,4,6-trimethylphenyl group or a 2,6-diisopropylphenyl group, and

$R^3$  and  $R^4$  are each, independently, a hydrogen atom, a halogen atom, or a hydrocarbyl group,

and wherein the molar ratio of metal atoms of the metal compound to aryl halide or aryl pseudohalide molecules is in the range of from about 0.01:1 to about 0.10:1.

74. A process according to Claim 59 wherein said N-heterocyclic carbene is a protonated salt of a bis(imidazoline-2-ylidene) of the formula



wherein

$R^1$  and  $R^2$  are the same, and each is a 2,4,6-trimethylphenyl group or a 2,6-diisopropylphenyl group,

$R^3$  and  $R^4$  are each, independently, a hydrogen atom, a halogen atom, or a hydrocarbyl group,

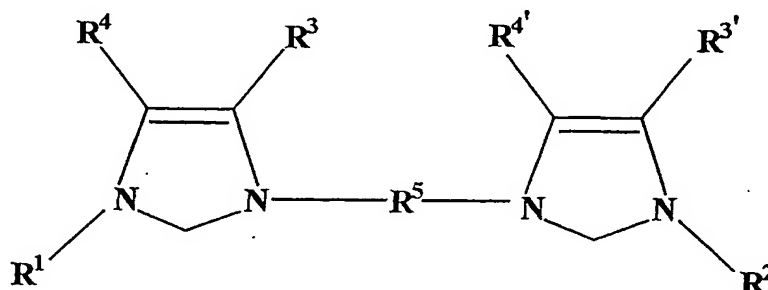
$R^{3'}$  and  $R^{4'}$  are as defined for  $R^3$  and  $R^4$ , and

$R^5$  is a bridging group that links the two imidazoline rings,

and wherein said strong base is a cesium salt and wherein said metal compound is a palladium compound.

75. A process according to Claim 74 wherein said cesium salt is cesium fluoride and wherein said palladium compound is palladium acetate.

76. A process according to Claim 59 wherein said N-heterocyclic carbene is a protonated salt of a bis(imidazoline-2-ylidene) of the formula



wherein

R1 and R2 are the same, and each is a 2,4,6-trimethylphenyl group or a 2,6-diisopropylphenyl group,

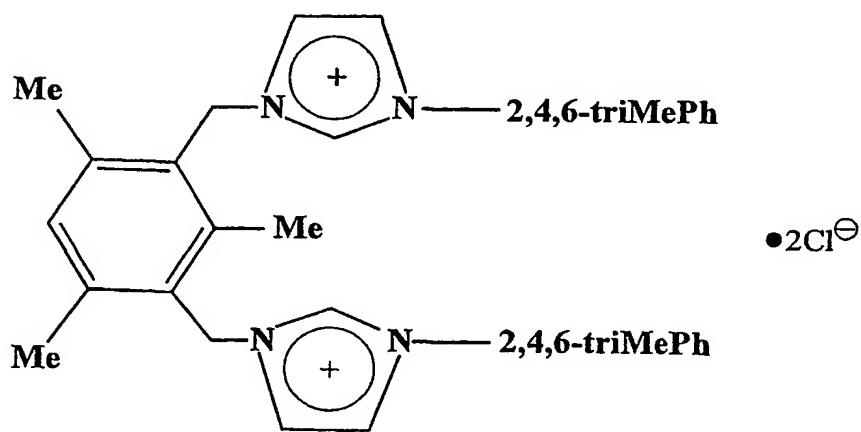
R3 and R4 are each, independently, a hydrogen atom, a halogen atom, or a hydrocarbyl group,

R3' and R4' are as defined for R3 and R4, and

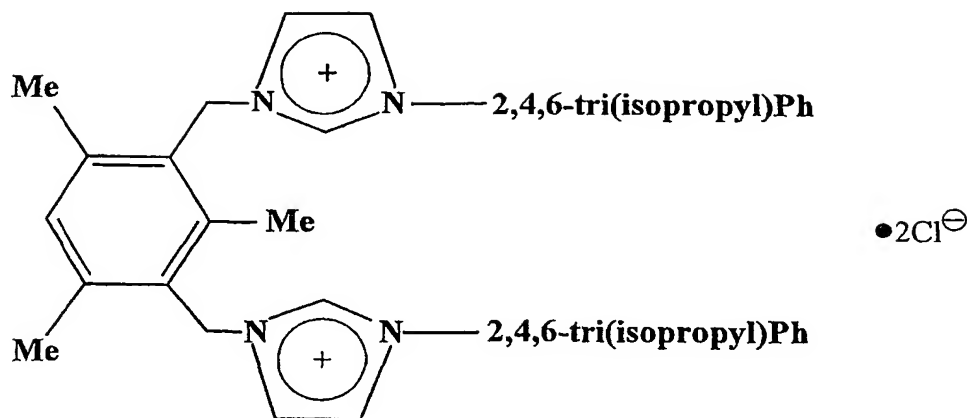
R5 is a bridging group that links the two imidazoline rings,

and wherein the molar ratio of metal atoms of the metal compound to aryl halide or aryl pseudohalide molecules is in the range of from about 0.01:1 to about 0.10:1.

77. A process according to Claim 59 wherein said N-heterocyclic carbene is



or



78. A process according to Claim 59 wherein the molar ratio of metal atoms of the metal compound to aryl halide or aryl pseudohalide molecules is in the range of from about 0.01:1 to about 0.10:1.

79. A process according to Claim 59 wherein a salt additive is also mixed in the liquid medium.

80. A process according to Claim 79 wherein said salt additive is an alkali metal halide.

81. A process according to Claim 80 wherein said alkali metal halide is either lithium chloride or sodium iodide.

82. A process according to Claim 1 wherein said transmetalating agent is at least one silane wherein the silicon atom is quaternary, wherein one group bound to the silicon atom is unsaturated at the alpha or beta position, and wherein each of the remaining groups bound to the silicon atom is a saturated hydrocarbyl or a saturated hydrocarbyloxy group.

83. A process according to Claim 82 wherein said aryl halide or aryl pseudohalide is selected from the group consisting of methyl-4-chlorobenzoate, 4-chlorobenzonitrile, 4-chloroacetophenone, and 4-chlorotoluene.

84. A process according to Claim 82 wherein said aryl halide or aryl pseudohalide is an aryl bromide.

85. A process according to Claim 84 wherein said aryl chloride is selected from the group consisting of methyl-4-bromobenzoate, 4-bromobenzonitrile, 4-

bromoacetophenone, and 4-bromotoluene.

86. A process according to Claim 82 wherein said aryl halide or aryl pseudohalide is a heteroaryl halide.

87. A process according to Claim 86 wherein said heteroaryl halide is a pyridine halide.

88. A process according to Claim 87 wherein said heteroaryl halide is either 2-chloropyridine or 2-bromopyridine.

89. A process according to Claim 82 wherein said aryl halide or aryl pseudohalide is an aryl toluenesulfonate.

90. A process according to Claim 82 wherein said aryl halide or aryl pseudohalide is an aryl trifluoromethanesulfonate.

91. A process according to Claim 82 wherein said aryl halide or aryl pseudohalide is a phenyl halide or phenyl pseudohalide.

92. A process according to Claim 91 wherein said phenyl halide or phenyl pseudohalide is chlorobenzene.

93. A process according to Claim 82 wherein said unsaturated group of the silane is a phenyl group.

94. A process according to Claim 93 wherein said silane is selected from the group consisting of phenyltrimethylsilane, phenyltrimethoxysilane, and triethyl(pentafluorophenyl)silane.

95. A process according to Claim 82 wherein said unsaturated group of the silane is a naphthyl group.

96. A process according to Claim 95 wherein said silane is either (6-methoxy-2-naphthyl)trimethoxysilane or (6-methoxy-2-naphthyl)trimethylsilane.

97. A process according to Claim 82 wherein said unsaturated group of the silane is a vinyl group.

98. A process according to Claim 97 wherein said silane is either (vinyl)trimethylsilane or (vinyl)trimethoxysilane.

99. A process according to Claim 82 wherein said unsaturated group of the silane is an allyl group.

100. A process according to Claim 99 wherein said silane is either

(allyl)trimethylsilane or (allyl)trimethoxysilane.

101. A process according to Claim 82 wherein said strong base is tetrabutylammonium fluoride.

102. A process according to Claim 82 wherein said strong base is a fluoride salt.

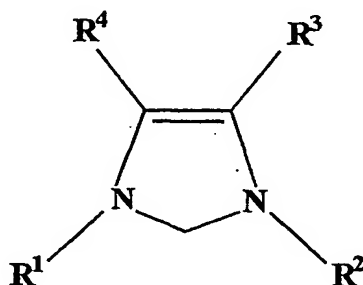
103. A process according to Claim 102 wherein said fluoride salt is an ammonium fluoride salt.

104. A process according to Claim 103 wherein said salt is selected from the group consisting of tetramethylammonium fluoride, tetrabutylammonium fluoride, and tetraoctylammonium fluoride.

105. A process according to Claim 82 wherein said strong base is tetrabutylammonium fluoride, wherein the metal compound is selected from the group consisting of palladium acetate, palladium chloride, and dipalladium tris(dibenzylideneacetone), and wherein the aryl halide or aryl pseudohalide is an aryl chloride.

106. A process according to Claim 82 wherein said strong base is either tetraoctylammonium fluoride or tetrabutylammonium fluoride, wherein the metal compound is selected from the group consisting of palladium acetate, palladium chloride, and dipalladium tris(dibenzylideneacetone), and wherein the aryl halide or aryl pseudohalide is either an aryl trifluoromethanesulfonate or an aryl toluenesulfonate.

107. A process according to Claim 82 wherein said N-heterocyclic carbene is an imidazoline-2-ylidene of the formula



or a protonated salt thereof, wherein

R<sup>1</sup> and R<sup>2</sup> are the same, and each is either a 2,4,6-trimethylphenyl group or a

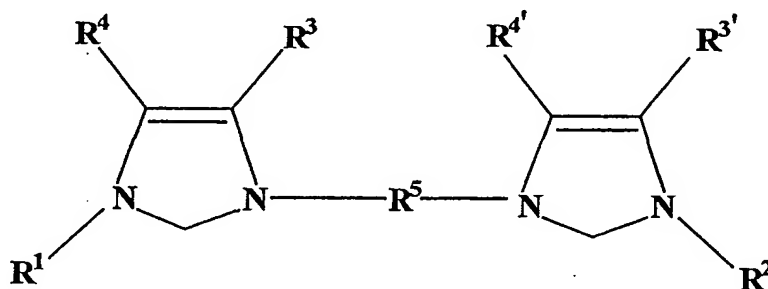
2,6-diisopropylphenyl group, and

R<sup>3</sup> and R<sup>4</sup> are each, independently, a hydrogen atom, a halogen atom, or a hydrocarbyl group,

and wherein said strong base is an ammonium fluoride salt and said metal compound is a palladium compound.

108. A process according to Claim 107 wherein said fluoride salt is tetrabutylammonium fluoride, and wherein said palladium compound is selected from the group consisting of palladium acetate, palladium chloride, and dipalladium tris(dibenzylideneacetone).

109. A process according to Claim 82 wherein said N-heterocyclic carbene is a protonated salt of a bis(imidazoline-2-ylidene) of the formula



wherein

R1 and R2 are the same, and each is a 2,4,6-trimethylphenyl group or a 2,6-diisopropylphenyl group,

R3 and R4 are each, independently, a hydrogen atom, a halogen atom, or a hydrocarbyl group,

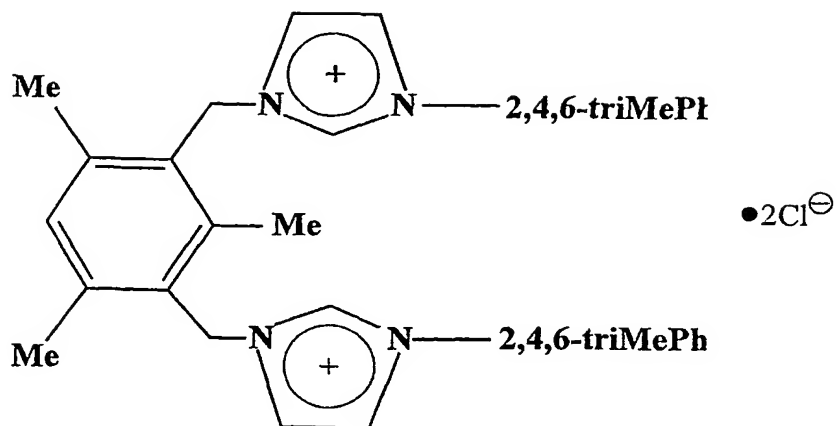
R3' and R4' are as defined for R3 and R4, and

R5 is a bridging group that links the two imidazoline rings,

and wherein said strong base is an ammonium fluoride salt and said metal compound is a palladium compound.

110. A process according to Claim 109 wherein said fluoride salt is tetrabutylammonium fluoride, and wherein said palladium compound is palladium acetate.

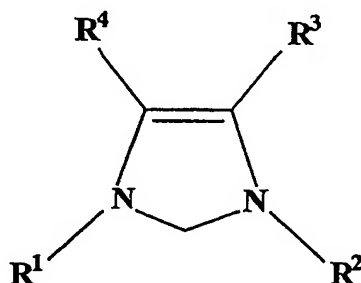
111. A process according to Claim 82 wherein said N-heterocyclic carbene is



112. A process according to Claim 82 wherein the molar ratio of aryl halide or aryl pseudohalide to silane is in the range of from about 1:1.5 to about 1:4.

113. A process according to Claim 82 wherein said aryl halide or aryl pseudohalide is either an aryl bromide or an aryl iodide, and wherein the temperature is in the range of from about 20°C to about 90°C.

114. A process according to any of Claims 2, 16, 36, 59 and 82 wherein said N-heterocyclic carbene is an imidazoline-2-ylidene of the formula



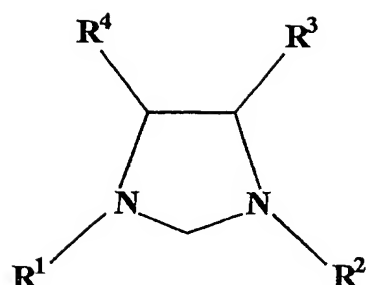
or a protonated salt thereof, wherein

$\text{R}^1$  and  $\text{R}^2$  are each, independently, alkyl or aryl groups having at least 3 carbon atoms, and

$\text{R}^3$  and  $\text{R}^4$  are each, independently, a hydrogen atom, a halogen atom, or a hydrocarbyl group.

115. A process according to any of Claims 2, 16, 36, 59 and 82 wherein said N-heterocyclic carbene is an imidazolidine-2-ylidene of the formula



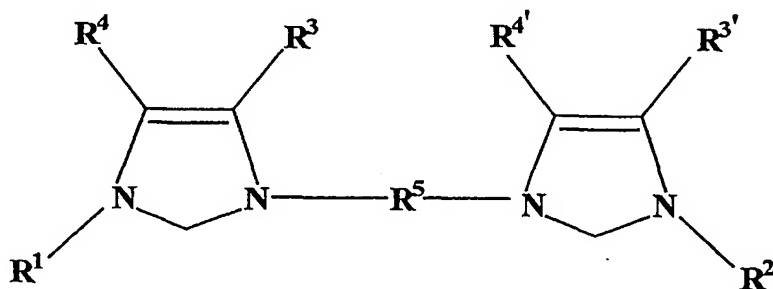


or a protonated salt thereof, wherein

$R^1$  and  $R^2$  are each, independently, alkyl or aryl groups having at least 3 carbon atoms, and

$R^3$  and  $R^4$  are each, independently, a hydrogen atom, a halogen atom, or a hydrocarbyl group.

116. A process according to any of Claims 2, 16, 36, 59 and 82 wherein said N-heterocyclic carbene is a bis(imidazoline-2-ylidene) of the formula



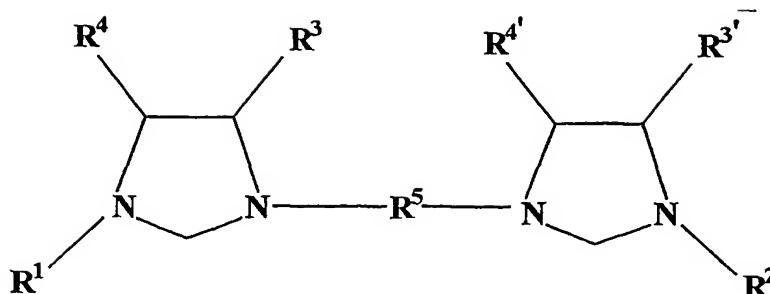
or a protonated salt thereof, wherein

$R^1$  and  $R^2$  are each, independently, alkyl or aryl groups having at least 3 carbon atoms,  $R^3$  and  $R^4$  are each, independently, a hydrogen atom, a halogen atom, or a hydrocarbyl group,

$R^{3'}$  and  $R^{4'}$  are as defined for  $R^3$  and  $R^4$ , and

$R^5$  is a bridging group that links the two imidazoline rings.

117. A process according to any of Claims 2, 16, 36, 59 and 82 wherein said N-heterocyclic carbene is a bis(imidazolidine-2-ylidene) of the formula



or a protonated salt thereof, wherein

$R^1$  and  $R^2$  are each, independently, alkyl or aryl groups having at least 3 carbon atoms,  $R^3$  and  $R^4$  are each, independently, a hydrogen atom, a halogen atom, or a hydrocarbyl group,

$R^{3'}$  and  $R^{4'}$  are as defined for  $R^3$  and  $R^4$ , and

$R^5$  is a bridging group that links the two imidazoline rings.

118. A process according to any one of Claims 2, 16, 36, 59 and 82 wherein said liquid medium comprises at least one ether.

119. A process according to Claim 118 wherein said ether is a cyclic ether.

120. A process according to Claim 119 wherein said ether is 1,4-dioxane.

121. A process according to any of Claims 2, 16, 36, 59 and 82 wherein said aryl halide or aryl pseudohalide is an aryl chloride.

122. A process according to Claim 121 wherein said aryl chloride is selected from the group consisting of 4-chlorotoluene, 1-methoxy-4-chlorobenzene, 1,4-dimethyl-2-chlorobenzene, and methyl-4-chlorobenzoate.

123. A process according to any of Claims 2, 16, 59 and 82 wherein said aryl halide or aryl pseudohalide is an aryl toluenesulfonate.

124. A process according to any of Claims 2, 16, 59 and 82 wherein said aryl halide or aryl pseudohalide is an aryl trifluoromethanesulfonate.

125. A process according to Claim 124 wherein said aryl trifluoromethanesulfonate is either 1-methoxy-4-(trifluoromethanesulfonate)benzene or methyl-4-(trifluoromethanesulfonate)benzoate.

126. A process according to any of Claims 2, 16, 59 and 82 wherein said aryl halide or aryl pseudohalide is a phenyl halide or phenyl pseudohalide.

127. A process according to Claim 126 wherein said phenyl halide or phenyl pseudohalide is chlorobenzene.
128. A process according to any of Claims 2, 16, 59 and 82 wherein said aryl halide or aryl pseudohalide is a naphthyl halide or naphthyl pseudohalide.
129. A process according to any of Claims 2, 59 and 82 wherein said naphthyl halide or naphthyl pseudohalide is 2-bromonaphthalene.
130. A process according to either of Claims 16, 36 and 82 wherein said aryl halide or aryl pseudohalide is an aryl bromide.
131. A process according to any of Claims 2, 16, 36, 59 and 82 wherein said metal compound comprises a palladium compound.
132. A process according to Claim 131 wherein said palladium compound is selected from the group consisting of palladium acetate, palladium chloride, and dipalladium tris(dibenzylideneacetone).
133. A process according to any of Claims 2, 16, 36, 59 and 82 wherein said metal compound comprises a nickel compound.
134. A process according to Claim 133 wherein said nickel compound is bis(1,5-cyclooctadiene)nickel.
135. A process according to any of Claims 2, 16, and 59 wherein said metal compound is bis(1,5-cyclooctadiene)nickel and wherein said strong base is cesium carbonate.
136. A process according to any of Claims 2, 16 and 59 wherein said strong base is an alkali metal salt.
137. A process according to Claim 136 wherein said alkali metal salt is either a potassium salt or a cesium salt.
138. A process according to either of Claims 16 and 59 said strong base is an alkali metal salt selected from the group consisting of potassium carbonate, potassium tert-butoxide, cesium carbonate, and cesium fluoride.
139. A process according to any of Claims 2, 16, 36, 59 and 82 wherein said N-heterocyclic carbene is an imidazoline-2-ylidene or a protonated salt thereof.
140. A process according to Claim 114 wherein  $R^1$  and  $R^2$  of said N-heterocyclic carbene are the same, and each is either a 2,4,6-trimethylphenyl group or a 2,6-diisopropylphenyl group.

141. A process according to Claim 115 wherein  $R^1$  and  $R^2$  of said N-heterocyclic carbene are the same, and each is either a 2,4,6-trimethylphenyl group or a 2,6-diisopropylphenyl group.

142. A process according to Claim 116 wherein  $R^1$  and  $R^2$  of said N-heterocyclic carbene are the same, and each is either a 2,4,6-trimethylphenyl group or a 2,6-diisopropylphenyl group.

143. A process according to Claim 117 wherein  $R^1$  and  $R^2$  of said N-heterocyclic carbene are the same, and each is either a 2,4,6-trimethylphenyl group or a 2,6-diisopropylphenyl group.

144. A process according to Claim 140 wherein said N-heterocyclic carbene is a protonated salt of an imidazoline-2-ylidene.

145. A process according to Claim 114 wherein  $R^3$  and  $R^4$  of said N-heterocyclic carbene are the same, and each is a hydrogen atom.

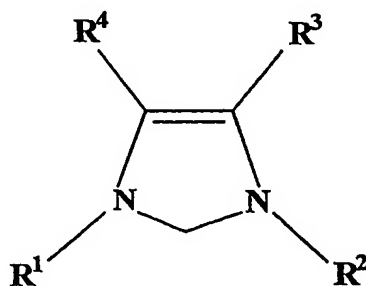
146. A process according to Claim 115 wherein  $R^3$  and  $R^4$  of said N-heterocyclic carbene are the same, and each is a hydrogen atom.

147. A process according to Claim 116 wherein  $R^3$  and  $R^4$  of said N-heterocyclic carbene are the same, and each is a hydrogen atom.

148. A process according to Claim 117 wherein  $R^3$  and  $R^4$  of said N-heterocyclic carbene are the same, and each is a hydrogen atom.

149. A process according to Claim 140 wherein  $R^3$  and  $R^4$  of said N-heterocyclic carbene are the same, and each is a hydrogen atom.

150. A process according to any of Claims 2, 16, 36 and 82 wherein said N-heterocyclic carbene is an imidazoline-2-ylidene of the formula



or a protonated salt thereof,  
wherein

$R^1$  and  $R^2$  are the same, and each is either a 2,4,6-trimethylphenyl group or a

2,6-diisopropylphenyl group, and

$R^3$  and  $R^4$  are each, independently, a hydrogen atom, a halogen atom, or a hydrocarbyl group,

and wherein the molar ratio of metal atoms of the metal compound to aryl halide or aryl pseudohalide molecules is in the range of from about 0.01:1 to about 0.05:1.

151. A process according to Claim 116 wherein said N-heterocyclic carbene is a protonated salt of a bis(imidazoline-2-ylidene).

152. A process according to Claim 151 wherein  $R^1$  and  $R^2$  of said protonated salt are the same, and each is selected from the group consisting of a 2,4,6-trimethylphenyl group, a 2,6-diisopropylphenyl group and a 2,4,6-triisopropylphenyl group.

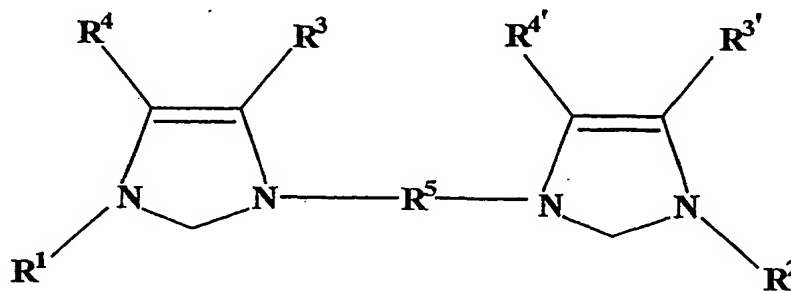
153. A process according to Claim 151 wherein  $R^{3'}$  and  $R^{4'}$  of said protonated salt are the same, and each is a hydrogen atom.

154. A process according to Claim 116 wherein  $R^{3'}$  and  $R^{4'}$  of said N-heterocyclic carbene are the same, and each is a hydrogen atom.

155. A process according to Claim 117 wherein  $R^{3'}$  and  $R^{4'}$  of said N-heterocyclic carbene are hydrogen atoms.

156. A process according to Claim 151 wherein  $R^3$  and  $R^4$  of said protonated salt are the same, and each is a hydrogen atom.

157. A process according to any of Claims 2, 16, 36 and 82 wherein said N-heterocyclic carbene is a protonated salt of a bis(imidazoline-2-ylidene) of the formula



wherein

$R^1$  and  $R^2$  are the same, and each is either a 2,4,6-trimethylphenyl group or a 2,6-diisopropylphenyl group, and

$R^3$  and  $R^4$  are each, independently, a hydrogen atom, a halogen atom, or a hydrocarbyl

group,

$R^{3'}$  and  $R^{4'}$  are as defined for  $R^3$  and  $R^4$ , and

$R^5$  is a bridging group that links the two imidazoline rings,  
and wherein the molar ratio of metal atoms of the metal compound to aryl halide or aryl pseudohalide molecules is in the range of from about 0.01:1 to about 0.05:1.

158. A process according to Claim 116 wherein the bridge formed by  $R^5$  has at least four atoms.

159. A process according to Claim 158 wherein the bridge formed by  $R^5$  has four to eight atoms.

160. A process according to Claim 117 wherein the bridge formed by  $R^5$  has four to eight atoms.

161. A process according to Claim 116 wherein  $R^5$  is a substituted benzo moiety.

162. A process according to Claim 118 wherein  $R^5$  is a substituted benzo moiety.

163. A process according to any of Claims 2, 16 and 59 wherein the molar ratio of aryl halide or aryl pseudohalide to transmetalating agent is in the range of from about 1:1 to about 1:3.

164. A process according to any of Claims 2, 16, 59 and 82 wherein the molar ratio of aryl halide or aryl pseudohalide to strong base is in the range of from about 1:1 to about 1:5.

165. A process according to any of Claims 2, 16, 36 and 82 wherein the molar ratio of metal atoms of the metal compound to aryl halide or aryl pseudohalide molecules is in the range of from about 0.01:1 to about 0.05:1.

166. A process according to any of Claims 2, 16, 36, 59 and 82 wherein the molar ratio of metal atoms of the metal compound to N-heterocyclic carbene is in the range of from about 1:0.5 to about 1:5.

167. A process according to any of Claims 2, 16, 36, 59 and 82 wherein the temperature is in the range of from about 20°C to about 150°C.

168. A process according to either of Claims 2 and 82 wherein the temperature is in the range of from about 20°C to about 110°C.

169. A process according to either of Claims 16 and 59 wherein the temperature is

in the range of from about 20°C to about 120°C.

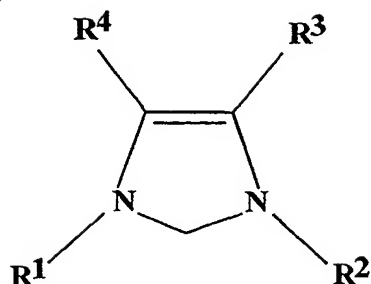
170. A process according to any of Claims 2, 16, 59 and 82 wherein said aryl halide or aryl pseudohalide is selected from the group consisting of an aryl chloride, an aryl tosylate, and an aryl triflate, and wherein the temperature is in the range of from about 40°C to about 150°C.

171. A process according to Claims 2, 16 and 59 wherein said aryl halide or aryl pseudohalide is either an aryl bromide or an aryl iodide, and wherein the temperature is in the range of from about 20°C to about 70°C.

172. A process which comprises mixing, in a liquid medium

- i) at least one aryl pseudohalide;
- ii) at least one metal compound comprising at least one metal atom selected from nickel, palladium, and platinum, wherein the formal oxidation state of the metal is zero or two; and
- iii) at least one N-heterocyclic carbene selected from the group consisting of an imidazoline-2-ylidene wherein the 1 and 3 positions are each, independently, substituted by a secondary or tertiary group which has at least three atoms, or a protonated salt thereof; an imidazolidine-2-ylidene wherein the 1 and 3 positions are each, independently, substituted by a secondary or tertiary group which has at least three atoms, or a protonated salt thereof; a bis(imidazoline-2-ylidene) wherein a bridging moiety is bound to one nitrogen atom of each ring, and wherein the remaining two nitrogen atoms are each, independently, substituted by a secondary or tertiary group which has at least three atoms, or a protonated salt thereof; and a bis(imidazolidine-2-ylidene) wherein a bridging moiety is bound to one nitrogen atom of each ring, and wherein the remaining two nitrogen atoms are each, independently, substituted by a secondary or tertiary group which has at least three atoms, or a protonated salt thereof, and mixtures of two or more of the foregoing.

173. A process according to Claim 172 wherein said N-heterocyclic carbene is an imidazoline-2-ylidene of the formula



or a protonated salt thereof, wherein

R1 and R2 are each, independently, alkyl or aryl groups having at least 3 carbon atoms, and

R3 and R4 are each, independently, a hydrogen atom, a halogen atom, or a hydrocarbyl group.

174. A process according to Claim 172 wherein said liquid medium comprises at least one ether.

175. A process according to Claim 174 wherein said ether is 1,4-dioxane.

176. A process according to Claim 172 wherein said aryl pseudohalide is an aryl trifluoromethanesulfonate.

177. A process according to Claim 172 wherein said aryl pseudohalide is an aryl toluene sulfonate.

178. A process according to Claim 172 wherein said aryl pseudohalide is selected from the group consisting of 4-methylphenyl trifluoromethanesulfonate, 4-methoxyphenyl trifluoromethanesulfonate, and 4-methoxyphenyl(toluene sulfonate).

179. A process according to Claim 172 wherein a Grignard reagent is also mixed in the liquid medium.

180. A process according to Claim 179 wherein said Grignard reagent is phenylmagnesium halide.

181. A process according to Claim 172 wherein said metal compound comprises a palladium compound.

182. A process according to Claim 181 wherein said palladium compound is dipalladium tris(dibenzylideneacetone).

183. A process according to Claim 173 wherein R1 and R2 of said N-heterocyclic



carbene are the same, and each is a 2,4,6-trimethylphenyl group or a 2,6-diisopropylphenyl group, and wherein R3 and R4 of said N-heterocyclic carbene are the same, and each is a hydrogen atom.

184. A process according to Claim 172 wherein the molar ratio of metal atoms of the metal compound to aryl pseudohalide molecules is in the range of from about 0.01:1 to about 0.05:1, and wherein the molar ratio of metal atoms of the metal compound to N-heterocyclic carbene is in the range of from about 1:0.5 to about 1:5.

185. A composition which comprises

- a) at least one metal compound comprising at least one transition metal atom; and
  - b) at least one N-heterocyclic carbene selected from the group consisting of
    - i) an imidazoline-2-ylidene wherein the 1 and 3 positions are each, independently, substituted by an aromatic group in which each ortho position is, independently, substituted by a secondary or tertiary group which has at least three atoms, or a protonated salt of such an imidazoline-2-ylidene;
    - ii) an imidazolidine-2-ylidene wherein the 1 and 3 positions are each, independently, substituted by an aromatic group in which each ortho position is, independently, substituted by a secondary or tertiary group having at least three atoms, or a protonated salt of such an imidazolidine-2-ylidene;
    - iii) a bis(imidazoline-2-ylidene) wherein a bridging moiety is bound to one nitrogen atom of each ring, wherein the bridge formed by the bridging moiety has at least five atoms, and wherein the remaining two nitrogen atoms are each, independently, substituted by a secondary or tertiary group which has at least three atoms, or a protonated salt of such a bis(imidazoline-2-ylidene);
    - iv) a bis(imidazolidine-2-ylidene) wherein a bridging moiety is bound to one nitrogen atom of each ring, wherein the bridge formed by the bridging moiety has at least five atoms, and wherein the remaining two nitrogen atoms are each, independently, substituted by a secondary or tertiary group which has at least three atoms, or a protonated salt of such a bis(imidazolidine-2-ylidene);
- and mixtures of two or more of the foregoing.

186. A composition according to Claim 185 wherein said transition metal is selected from Groups 8-11 of the Periodic Table.

187. A composition according to Claim 185 wherein said transition metal is selected from Group 10 of the Periodic Table.

188. A composition according to Claim 185 wherein said metal compound is either a nickel compound or a palladium compound.

189. A composition according to Claim 188 wherein the formal oxidation state of the metal is zero or two.

190. A composition according to Claim 188 wherein said metal compound is a palladium compound, and is selected from the group consisting of palladium chloride, palladium acetate or dipalladium tris(dibenzylideneacetone).

191. A composition according to Claim 188 wherein said metal compound is a nickel compound, and is bis(1,5-cyclooctadiene)nickel.

192. A composition according to Claim 185 wherein said N-heterocyclic carbene is selected from the group consisting of an imidazoline-2-ylidene, an imidazolidine-2-ylidene, a protonated salt of an imidazoline-2-ylidene, and a protonated salt of an imidazolidine-2-ylidene; wherein said aromatic groups are the same, and each is a 2,6-diisopropylphenyl group; and wherein said metal compound is selected from the group consisting of bis(1,5-cyclooctadiene)nickel, palladium chloride, palladium acetate, and dipalladium tris(dibenzylideneacetone).

193. A composition according to Claim 185 wherein said N-heterocyclic carbene is selected from the group consisting of a bis(imidazoline-2-ylidene), a bis(imidazolidine-2-ylidene), a protonated salt of a bis(imidazoline-2-ylidene), and a protonated salt of a bis(imidazolidine-2-ylidene); wherein said secondary or tertiary group on the remaining two nitrogen atoms are the same, and each is a substituted phenyl moiety selected from the group consisting of a 2,4,6-trimethylphenyl group, a 2,6-diisopropylphenyl group, and a 2,4,6-triisopropylphenyl group.

194. A composition according to Claim 193 wherein the bridging moiety is a biphenylene, binaphthylene, benzo, or substituted benzo moiety.

195. A composition according to Claim 194 wherein said metal compound is selected from the group consisting of bis(1,5-cyclooctadiene)nickel, palladium chloride, palladium acetate and dipalladium tris(dibenzylideneacetone).

196. A composition which comprises

at least one N-heterocyclic carbene selected from the group consisting of

- i) an imidazoline-2-ylidene wherein the 1 and 3 positions are each, independently, substituted by an aromatic group in which each ortho position is, independently, substituted by a secondary or tertiary group which has at least three atoms, or a protonated salt of such an imidazoline-2-ylidene;
- ii) an imidazolidine-2-ylidene wherein the 1 and 3 positions are each, independently, substituted by an aromatic group in which each ortho position is, independently, substituted by a secondary or tertiary group having at least three atoms, or a protonated salt of such an imidazolidine-2-ylidene;
- iii) a bis(imidazoline-2-ylidene) wherein a bridging moiety is bound to one nitrogen atom of each ring, wherein the bridge formed by the bridging moiety has at least five atoms, and wherein the remaining two nitrogen atoms are each, independently, substituted by a secondary or tertiary group which has at least three atoms, or a protonated salt of such a bis(imidazoline-2-ylidene);
- iv) a bis(imidazolidine-2-ylidene) wherein a bridging moiety is bound to one nitrogen atom of each ring, wherein the bridge formed by the bridging moiety has at least five atoms, and wherein the remaining two nitrogen atoms are each, independently, substituted by a secondary or tertiary group which has at least three atoms, or a protonated salt of such a bis(imidazolidine-2-ylidene);

and mixtures of two or more of the foregoing.

197. A composition according to either of Claims 185 and 196 wherein said N-heterocyclic carbene is selected from the group consisting of an imidazoline-2-ylidene, an imidazolidine-2-ylidene, a protonated salt of an imidazoline-2-ylidene, and a protonated salt of an imidazolidine-2-ylidene.

198. A composition according to Claim 197 wherein said secondary or tertiary group at the ortho position of the aromatic group has from three to about twelve carbon atoms.

199. A composition according to Claim 197 wherein said aromatic groups are the same, and each is a disubstituted phenyl group.

200. A composition according to Claim 199 wherein said disubstituted phenyl group is a 2,6-diisopropylphenyl group.

201. A composition according to Claim 200 wherein said N-heterocyclic carbene

is a protonated salt of a imidazoline-2-ylidene.

202. A composition according to either of Claims 185 and 196 wherein said N-heterocyclic carbene is selected from the group consisting of a bis(imidazoline-2-ylidene), a bis(imidazolidine-2-ylidene), a protonated salt of a bis(imidazoline-2-ylidene), and a protonated salt of a bis(imidazolidine-2-ylidene).

203. A composition according to Claim 202 wherein each said secondary or tertiary group on the remaining two nitrogen atoms has from three to about twelve carbon atoms.

204. A composition according to Claim 202 wherein said secondary or tertiary group on the remaining two nitrogen atoms are the same, and each is a substituted phenyl moiety.

205. A composition according to Claim 196 wherein said N-heterocyclic carbene is selected from the group consisting of a bis(imidazoline-2-ylidene), a bis(imidazolidine-2-ylidene), a protonated salt of a bis(imidazoline-2-ylidene), and a protonated salt of a bis(imidazolidine-2-ylidene); wherein said secondary or tertiary group on the remaining two nitrogen atoms are the same, and each is either a 2,4,6-trimethylphenyl group or a 2,6-diisopropylphenyl group.

206. A composition according to Claim 202 wherein said bridge has five to about eight atoms.

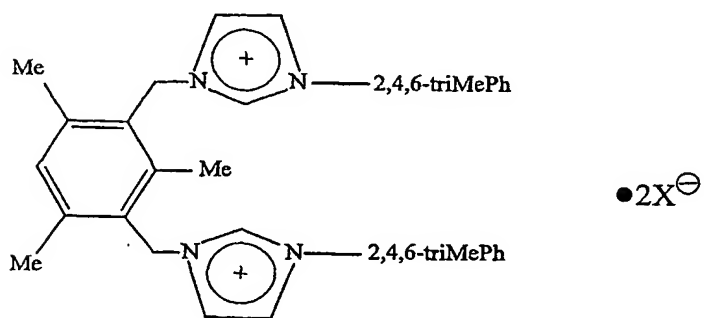
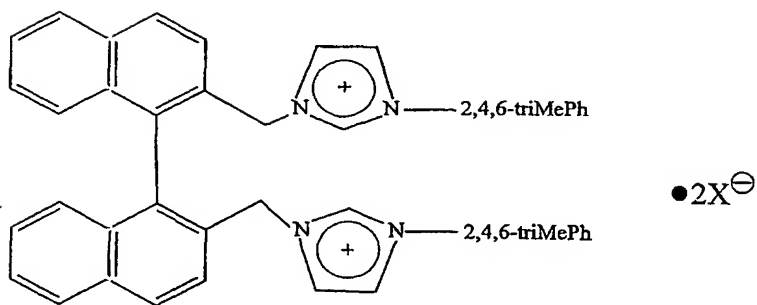
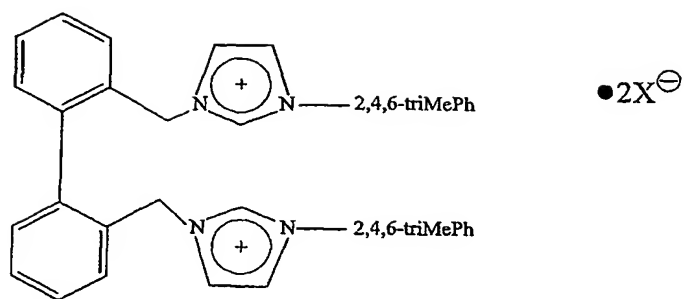
207. A composition according to Claim 202 wherein said bridging moiety has from about eight to about thirty carbon atoms.

208. A composition according to Claim 202 wherein the bridging moiety is a biphenylene, binaphthylene, benzo, or substituted benzo moiety.

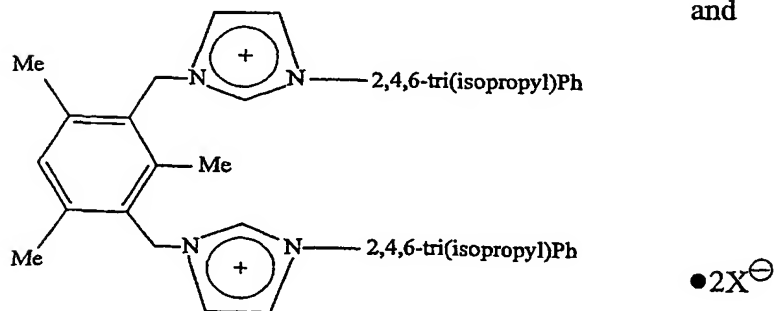
209. A composition according to Claim 205 wherein the bridging moiety is a biphenylene, binaphthylene, benzo, or substituted benzo moiety.

210. A composition according to Claim 208 wherein said N-heterocyclic carbene is a protonated salt of a bis(imidazoline-2-ylidene).

211. A composition according to Claim 210 wherein said protonated salt of the bis(imidazoline-2-ylidene) is selected from the group consisting of

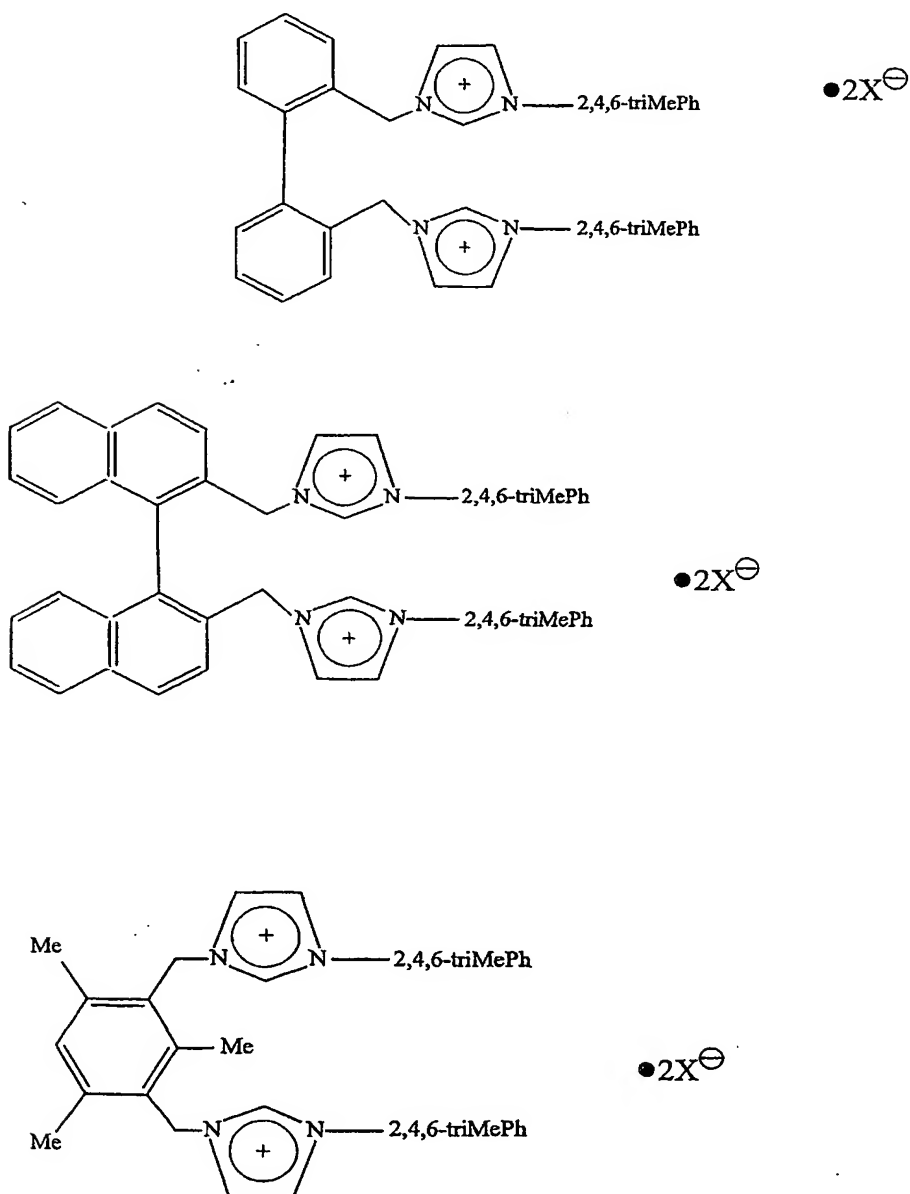


and

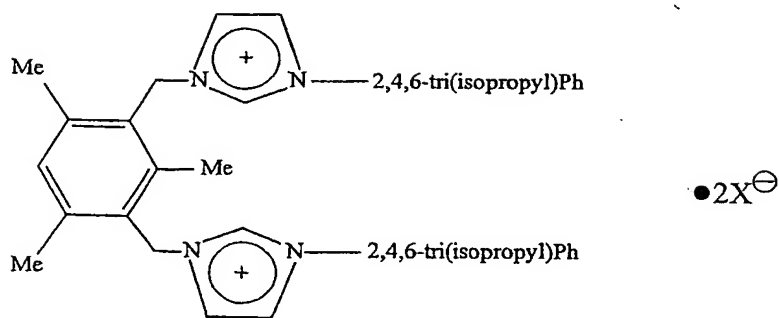


wherein X is a counterion.

212. A composition according to Claim 210 wherein said protonated salt of the bis(imidazoline-2-ylidene) is selected from the group consisting of

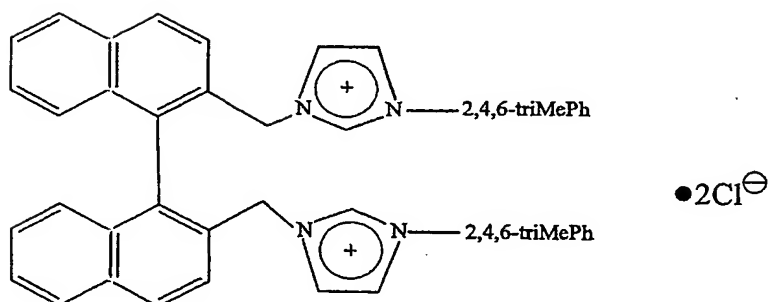
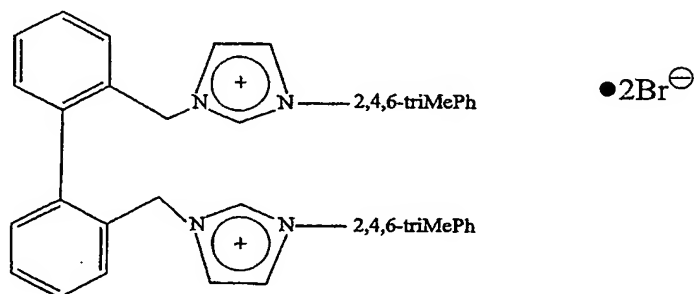


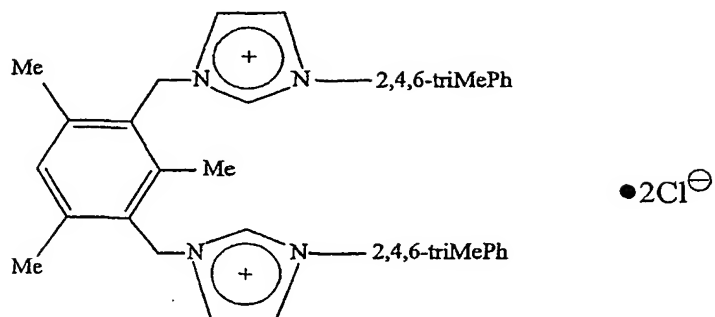
and



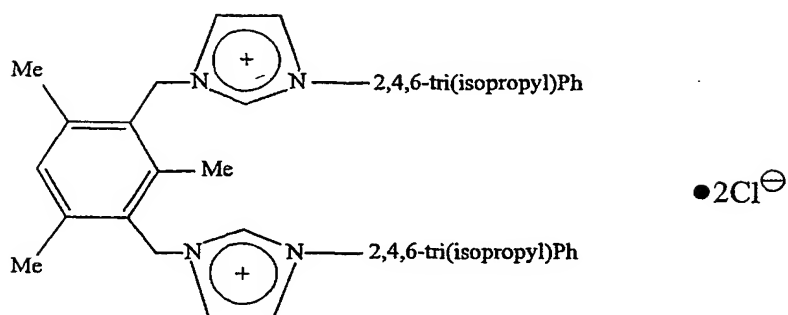
wherein X is a halide atom.

213. A composition according to Claim 210 wherein said protonated salt of the bis(imidazolinium-2-ylidene) is selected from the group consisting of





and



214. A composition according to Claim 196 further comprising a strong base.
215. A composition according to Claim 214 wherein said strong base is an alkali metal salt.
216. A composition according to Claim 215 wherein said alkali metal salt is selected from the group consisting of potassium carbonate, potassium *tert*-butoxide, cesium carbonate, and cesium fluoride.



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14 February 2002For two-letter codes and other abbreviations, refer to the "Guid-  
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ning of each regular issue of the PCT Gazette.

(54) Title: C-C AND C-N COUPLING CATALYST COMPRISING TRANSITION METAL AND CARBENE

(57) Abstract: This invention provides a process for conducting reactions to form carbon-to-carbon or carbon-to-nitrogen bonds. The processes of the present invention make use of N-heterocyclic carbenes as ancillary ligands in various types of couplings of aryl halides and/or aryl pseudohalides. A Suzuki coupling, for example, can be carried out by mixing, in a liquid medium, at least one strong base; at least one aryl halide or aryl pseudohalide in which all substituents are other than boronic acid groups, wherein the aryl halide has, directly bonded to the aromatic ring(s), at least one halogen atom selected from the group consisting of a chlorine atom, a bromine atom, and an iodine atom; at least one arylboronic acid in which all substituents are other than chlorine atoms, bromine atoms, iodine atoms, or pseudohalide groups; at least one metal compound comprising at least one metal atom selected from nickel, palladium, and platinum, wherein the formal oxidation state of the metal is zero or two; and at least one N-heterocyclic carbene. One preferred type of N-heterocyclic carbene is an imidazoline-2-ylidene of the formula (I) wherein R<sup>1</sup> and R<sup>2</sup> are each, independently, alkyl or aryl groups having at least 3 carbon atoms, R<sup>3</sup> and R<sup>4</sup> are each, independently, a hydrogen atom, a halogen atom, or a hydrocarbyl group.

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# INTERNATIONAL SEARCH REPORT

In tional Application No  
PCT/US 01/05549

## A. CLASSIFICATION OF SUBJECT MATTER

IPC 7 C07B37/04 C07B43/04 C07C209/10 C07D295/02 C07C1/32  
C07C43/20 C07C41/30 C07C69/76 C07C69/14

According to International Patent Classification (IPC) or to both national classification and IPC

## B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 7 C07B C07C C07D

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

EPO-Internal, CHEM ABS Data, BEILSTEIN Data

## C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 98 00399 A (DU PONT ;BAKER RALPH THOMAS (US); KRISTJANSDDTTIR SIGRIDUR SOLEY () 8 January 1998 (1998-01-08) the whole document	1-216
P,X	BÖHM ET AL: "Nickel-catalyzed cross-coupling of aryl chlorides with aryl grignard reagents" ANGEW. CHEM. INT. ED., vol. 39, no. 9, 2 May 2000 (2000-05-02), pages 1602-4, XP002178608 ligands 1 and 2 table 1	1-216



Further documents are listed in the continuation of box C.



Patent family members are listed in annex.

### \* Special categories of cited documents :

- \*A\* document defining the general state of the art which is not considered to be of particular relevance
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## INTERNATIONAL SEARCH REPORT

In International Application No

PCT/US 01/05549

## C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
P,X	BAKER ET AL.: "Palladium carbene complexes derived from imidazolium-linked ortho-cyclophanes" J. CHEM. SOC. DALTON TRANS., 21 January 2001 (2001-01-21), pages 111-20, XP002178609 Compounds 4-12 page 116, right-hand column, paragraph 3 table 4 ----	1-216
P,X	WESKAMP T ET AL: "Combining N-heterocyclic carbenes and phosphines: improved palladium(II) catalysts for aryl coupling reactions" JOURNAL OF ORGANOMETALLIC CHEMISTRY, ELSEVIER-SEQUOIA S.A. LAUSANNE, CH, vol. 585, no. 2, 15 August 1999 (1999-08-15), pages 348-352, XP004177479 ISSN: 0022-328X Compounds 1 and 2 table 1 ----	1-216
P,X	CADDICK ET AL.: "An improved synthesis of bis(1,3-di-N-tert-butylimidazol-2-ylidene) palladium(0) and its use in C-C and C-N coupling reactions" J. ORGANOMETALLIC CHEM., vol. 617-18, 15 January 2001 (2001-01-15), pages 635-9, XP002178610 Compound 1 Scheme 2 page 636, right-hand column, paragraph 3 -page 637, left-hand column, paragraph 2 ----	1-216
P,X	HERMANN ET AL.: "Synthesis, structure and catalytic application of Pd(II) complexes bearing N-heterocyclic carbenes and phosphines" J. ORGANOMETALLIC CHEM., vol. 617, no. 18, 15 January 2001 (2001-01-15), pages 616-28, XP002178611 Compounds 1,6 tables 2-5 ---- -/--	1-216

# INTERNATIONAL SEARCH REPORT

International Application No

PCT/US 01/05549

## C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
P, X	<p>BÖHM V P W ET AL: "N-Heterocyclic carbenes - Part 26. N-Heterocyclic carbene complexes of palladium(0): synthesis and application in the Suzuki cross-coupling reaction"</p> <p>JOURNAL OF ORGANOMETALLIC CHEMISTRY, ELSEVIER-SEQUOIA S.A. LAUSANNE, CH, vol. 595, no. 2, February 2000 (2000-02), pages 186-190, XP004187387</p> <p>ISSN: 0022-328X</p> <p>table 1</p> <p>Scheme 1</p>	1-216
A	<p>HERMANN ET AL: "Chelating N-heterocyclic carbene ligands in palladium-catalyzed heck-type reactions"</p> <p>JOURNAL OF ORGANOMETALLIC CHEMISTRY, ELSEVIER-SEQUOIA S.A. LAUSANNE, CH, vol. 557, no. 1, 20 April 1998 (1998-04-20), pages 93-96, XP004122368</p> <p>ISSN: 0022-328X</p> <p>cited in the application</p> <p>eq 2</p> <p>table 1</p> <p>Scheme 1</p>	1,172, 185,196
A	<p>WOLFGANG A. HERRMANN, CHRISTIAN KÖCHER: "N-Heterocyclic Carbenes"</p> <p>ANGEW. CHEM. INT. ED. ENGL., vol. 36, 1997, pages 2162-87, XP002178612</p> <p>5. Transition Metal Complexes</p> <p>page 2178, right-hand column</p> <p>7. Catalysis</p> <p>page 2181, right-hand column</p>	1,172, 185,196

## FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

Continuation of Box I.2

Claims Nos.: 172-182 (part.), 184-191 (part.), 196-197 (part.), 202-203 (part.), 206-210 (part.), 214-216 (part.)

Present claims 172-182 (part.), 184-191 (part.), 196-197 (part.), 202-203 (part.), 206-210 (part.), 214-216 (part.) relate to an extremely large number of possible processes and compositions. Support within the meaning of Article 6 PCT and/or disclosure within the meaning of Article 5 PCT is to be found, however, for only a very small proportion of the processes and compositions claimed. In the present case, the claims so lack support, and the application so lacks disclosure, that a meaningful search over the whole of the claimed scope is impossible. Consequently, the search has been carried out for those parts of the claims which appear to be supported and disclosed, namely those parts relating to the processes and compositions in which in all cases an aromatic group is attached to the nitrogen of the 1,3-diazole ring. This means that the search was carried out completely with respect to the above mentioned claims for:

- a) imidazoline-2-ylidene wherein the 1 and 3 position are both substituted by an aromatic ring (phenyl, naphthyl etc)
  - b) imidazolidine-2-ylidene wherein the 1 and 3 position are both substituted by an aromatic ring
  - c) bis(imidazoline-2-ylidene) wherein a bridging moiety (between 5 and 20 carbon atom) is bound to one nitrogen atom of each ring and to which an aromatic ring is attached to both other nitrogen atoms
  - d) bis(imidazolidine-2-ylidene) wherein a bridging moiety (between 5 and 20 carbon atom) is bound to one nitrogen atom of each ring and to which an aromatic ring is attached to both other nitrogen atoms.
- I.e. : in the search all examples of the present application were included.

Claims 1-171 could be searched completely.

The applicant's attention is drawn to the fact that claims, or parts of claims, relating to inventions in respect of which no international search report has been established need not be the subject of an international preliminary examination (Rule 66.1(e) PCT). The applicant is advised that the EPO policy when acting as an International Preliminary Examining Authority is normally not to carry out a preliminary examination on matter which has not been searched. This is the case irrespective of whether or not the claims are amended following receipt of the search report or during any Chapter II procedure.

# INTERNATIONAL SEARCH REPORT

Information on patent family members

Int. Application No

PCT/US 01/05549

Patent document cited in search report		Publication date	Patent family member(s)	Publication date
WO 9800399	A	08-01-1998	CA 2258594 A1	08-01-1998
			EP 0912510 A1	06-05-1999
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			WO 9800399 A1	08-01-1998
			US 6103937 A	15-08-2000

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